The Stochastic Human Exposure and Dose Simulation Model for Multimedia, Multipathway Chemicals (SHEDS-Multimedia):Dietary Module

SHEDS-Dietary version 1

Draft Technical Manual

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Disclaimer

EPA's SHEDS-Dietary model is a probabilistic, population-based dietary exposure assessment model that simulates individual exposures to chemicals in food and drinking water over different time periods (e.g., daily, yearly). SHEDS-Dietary is one module (along with the separate SHEDS-Residential module) of EPA's more comprehensive human exposure model, the Stochastic Human Exposure and Dose Simulation model for multimedia, multipathway chemicals (SHEDS-Multimedia), which can simulate aggregate or cumulative exposures over time via multiple routes of exposure (dietary & non-dietary) for different types of chemicals and scenarios. SHEDS-Residential and SHEDS-Dietary will be merged together in a future version of SHEDS-Multimedia.

SHEDS-Dietary version 1 includes case study examples for illustrative purposes, as described in the the Technical Manual and User Guide. All input values used in the SHEDS-Dietary model for a given application should be entered or reviewed by the researcher so that the model results are based on appropriate data sources for the given application.

The United States Environmental Protection Agency through its Office of Research and Development developed and funded the SHEDS-Dietary model with assistance from contractor Alion Science and Technology. SHEDS-Dietary Version 1 will undergo external peer review by EPA's Scientific Advisory Panel July, 2010, and should be considered draft at this time.

Acknowledgments

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Acronyms and Abbreviations

ai/kg bw	Active ingredient per kilogram body weight
ATUS	American Time Use Survey
CCA	Copper Chromated Arsenic
CHAD	Consolidated Human Activity Database
CRA	Cumulative Risk Assessment
CSFII	USDA Continuing Survey of Food Intakes by Individuals
CTEPP	Children's Total Exposure to Persistent Pollutants study
D &A	Diversity and Autocorrelation
DEEM	Dietary Exposure Evaluation Model
DWCS	Drinking Water Consumption Survey
EATS	Eating at America's Table Study
ERDEM	Exposure Related Dose Estimating Model
FCID	Food Commodity Intake Database
FDA	Food and Drug Administration
FF	Food form
FFQ	Food Frequency Question
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPQ	Food Quality Protection Act
LOD	Limit of detection
MEC	Mobile Examination Centers
NCI	National Cancer Institute
NHANES	National Health and Nutrition Survey
NMC	N-methyl carbamate insecticide
OP	Organophosphorous insecticide
OPP	Office of Pesticide Programs
PCT	Percent of crop treated
PD	Persisting Dose
PDP	USDA Pesticide Data Program
PRZM-EXAMS	Pesticide Root Zone Model – Exposure Analysis Modeling System
RAC	Raw agricultural commodity
SAP	Science Advisory Panel
SCIGROW	Screening Concentration in Ground Water
SHEDS	Stochastic Human Exposure and Dose Simulation
TDS	FDA Total Dietary Study
US EPA	United States Environmental Protection Agency
USDA	United States Department of Agriculture
WWEIA	NHANES what We Eat in America

1 Background

1.1 Purpose of SHEDS-Dietary

The EPA's Office of Pesticide Programs (OPP) is responsible for registering all uses of pesticides (http://www.epa.gov/pesticides/regulating/laws.htm.). The Agency must ensure that a pesticide, when used according to label directions, can be used with a reasonable certainty of no harm to human health and without posing unreasonable risks to the environment. The Agency also sets tolerances (maximum pesticide residue levels) for the amount of the pesticide that can legally remain in or on foods when a pesticide may be used on food or feed crops. Under the Food Quality and Protection Act of 1996 (FQPA), "the term 'safe', with respect to a tolerance for a pesticide chemical residue, means that the Administrator has determined that there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." FQPA specifies 'all anticipated dietary exposures' as the potential for concurrent exposures from 'all other tolerances in effect for the pesticide', and 'all other exposures' as the potential for concurrent exposures from 'non-occupational uses', such as lawn care and other residential uses of pesticides.

Since the passage of FQPA, the Agency has conducted three types of dietary risk assessments: acute (1-day), chronic, and cancer. Chronic and cancer risk assessments have been based traditionally on deterministic calculations at the per capita level, using DEEM-FCID™ to calculate exposure by combining food consumption and residue data (US EPA, FIFRA SAP 1997, 1998). For higher tier, refined acute dietary risk assessments, OPP has generally used DEEM-FCID (U.S. EPA 2000a) with Monte Carlo simulations to obtain an estimate of total daily dietary exposure to a pesticide. To conduct several cumulative risk assessments (OP CRA, NMC CRA, Triazine CRA), OPP has used longitudinal aggregate exposure models (e.g., Calendex-FCID, CARES, Lifeline), peer-reviewed by OPP's FIFRA SAP (U.S. EPA 1999, 2000b, 2000c, 2000d).

EPA's Office of Research and Development (ORD), National Exposure Research Laboratory (NERL) has developed the Stochastic Human Exposure and Dose (SHEDS)-Dietary model version 1 (v1), a probabilistic, population-based dietary exposure assessment model that simulates individual exposures to chemicals in food and drinking water over different time periods (e.g., daily, yearly) (Xue et al., 2010). SHEDS-Dietary is a module, along with SHEDS-Residential, of ORD/NERL's more comprehensive human exposure model, SHEDS-Multimedia (Zartarian et al., 2008; http://www.epa.gov/heasd/products/sheds_multimedia/sheds_mm.html; http://www.epa.gov/scipoly/SAP/meetings/2007/081407_mtg.htm).

The Stochastic Human Exposure and Dose Simulation model for multimedia, multiroute/pathway chemicals (SHEDS-Multimedia) is being developed as a state-of-science computer model for improving estimates of aggregate (single-chemical, multi-route/pathway) and cumulative (multi-chemical, multi-route/pathway) human exposure and dose. SHEDS-

Multimedia is the EPA/ORD's principal model for simulating human exposures to a variety of multimedia, multipathway environmental chemicals such as pesticides, metals, and persistent bioaccumulative toxins.

SHEDS-Multimedia version 4 is comprised of both the dietary module, SHEDS-Dietary version 1 (Xue, 2010) described in this technical manual and related user guide (Isaacs et al., 2010a), and a residential module, SHEDS-Residential version 4.0, described in a separate technical manual and user guide (Glen et al., 2010, Isaacs et al., 2010b). SHEDS-Residential is a physically-based, probabilistic model that predicts, for user-specified population cohorts, exposures incurred in the residential environment over time via inhaling contaminated air, touching contaminated surface residues, and ingesting residues from hand- or object- to-mouth activities. To do this, it combines information on chemical usage, human activity data (e.g., from time/activity diary surveys, videography studies), environmental residues and concentrations, and exposure factors to generate time series of exposure for simulated individuals. One-stage or two-stage Monte Carlo simulation is used to produce distributions of exposure for various population cohorts (e.g., age/gender groups) that reflect the variability and/or uncertainty in the input parameters.

A methodology for linking the residential and dietary modules for simulated individuals (based on age, gender, body weight, total caloric intake/METS, race, season, weekday and region) will be peer reviewed by EPA's July 20-22, 2010 FIFRA Scientific Advisory Panel. This methodology, described later in this manual in the section entitled, "Algorithm for Matching (Behavioral) Diaries: Food Consumption and Activity Patterns." has been tested through "soft linking" the two modules with a permethrin pesticide case study. In the next version of SHEDS-Multimedia, the dietary and residential module SAS codes will be merged, so that both types of exposure can be calculated for the same individual after food consumption and activity pattern diaries are appropriately matched. A common Graphical User Interface (GUI) will also allow the user to run either module separately, or to run them both together. The focus of this Technical Manual is the standalone SHEDS-Dietary model.

The SHEDS-Multimedia model, including the SHEDS-Dietary and SHEDS-Residential modules, represent an advancement in science over existing models, given some of the key features described below. SHEDS-Dietary allows conducting additional analyses for pesticides; quantifying uncertainty in acute dietary risk assessments; and enhancing chronic and cumulative risk assessments. This model can be applied to other chemicals as well as pesticides, and therefore may be useful to other Program Offices and Agencies.

This Technical Manual describes the algorithms, methodologies, data sources, and input and output options and capabilities of the SHEDS-Dietary model v1. ORD, in conjunction with OPP, developed this Agency state-of-the-science model to probabilistically estimate dietary exposures to inform regulatory risk assessments as well as address science questions for research purposes. ORD's SHEDS-Dietary modeling research focused on enhancing the science of probabilistic dietary exposure assessments. OPP collaboration on SHEDS-Dietary model development has considered criteria for regulatory use: peer-reviewed / transparent (algorithms); publicly available (free or nominal cost); and consistent with EPA/OPP policies and guidelines.

One major purpose of the July, 2010 FIFRA SAP meeting is to review SHEDS-Dietary version 1 and SHEDS-Residential (cumulative or aggregate) version 4 modules, and methodology for linking them in the next version of SHEDS-Multimedia, so they can be used for regulatory decision-making in EPA. Peer review of SHEDS-Multimedia, including its modules, methodologies, and case studies, is necessary for broad regulatory applications in EPA and potentially other Agencies. In 2007 the EPA FIFRA SAP reviewed the residential module of the SHEDS-Multimedia model (version 3), and provided peer consult of the conceptual dietary module (http://www.epa.gov/scipoly/SAP/meetings/2007/081407_mtg.htm).

SHEDS-Dietary is a publicly available, transparent model that uses the SAS platform (requires a SAS license for version 9.1 and higher); see specific computer requirements in the User Guide, Isaacs et al., 2010a), which provides model adaptability and the ability to view, query, analyze, and update the underlying databases (e.g., food consumption, recipes, residues). It also facilitates food consumption data (NHANES) and recipe updates, and development of alternate exposure modeling assumptions (e.g., stochastic assumption on residues, by eating occasion or day). SAS Output Tables provide flexibility to develop alternate contribution analyses, and facilitate linkage with PBPK models. This flexibility contributes to various features of SHEDS-Dietary to allow for exposure analyses in addition to standard dietary exposure model results (i.e., exposure at the 95th , 99th, and 99.9th percentiles of the population).

The SHEDS-Dietary model is consistent with EPA/OPP policies and guidelines in that it addresses FQPA requirements for acute and longitudinal aggregate and cumulative exposure assessments to pesticides residues in food, drinking water, and water used in food preparation while fulfilling the criteria described above for regulatory-use models.

The following sections of this manual describe the technical details of the SHEDS-Dietary model v1.

1.2 Overview of SHEDS-Dietary

SHEDS-Dietary can produce population percentiles of dietary exposure by source and age-gender group; quantify contribution to total exposure by food, commodity, and chemical; and be used for eating occasion, sensitivity, and uncertainty analyses. In general terms, it combines information about food and drinking water consumption data for each reported eating occasion with corresponding chemical residue/concentration data to estimate human dietary exposures. The model can use either USDA's Continuing Survey of Food Intake by Individuals (CSFII) (1994-96, 1998) or the NHANES/WWEIA (What We Eat in America) dietary consumption data (1999-2006), along with EPA/USDA recipe translation files (FCID; Food Commodity Intake Database), and available food and water concentration data. Specifics about combining this information require a number of technical considerations, such as translating foods reported as eaten into raw agricultural commodities using recipe files, sampling residues within a day and over time, considering non-detects, and allocating total drinking water consumption into within-day drinking water events. The goals of the SHEDS-Dietary model are to use state-of-the-science algorithms, to enhance the science of probabilistic dietary exposure assessments by allowing additional analyses, and to better characterize and quantify uncertainty in Agency risk assessments.

1.2.1 Key Features and Model Options

Some of the key features of SHEDS-Dietary are presented in Table 1-1 and described below:

Table 1-1 Key Features of SHEDS-Dietary

DS-Dietary Option/Feature	Available in SHEDS-Dietary?	Notes [Option linked to 2007 FIFRA SAP Question]
Food Consumption Data Sources		
CSFII (1994-96, 1998 Children supplemental)	Yes	Data used in Agency risk assessments (e.g., DEEM-FCID™)
NHANES (1999-2006), Preliminary data	Yes	Food recipes not available for new foods
Modeling Longitudinal Consumption (Food, Water) Patterns		
Within Day Direct DW Consumption: 6 Equal Amounts, Fixed Times (6 am, 9, 12, 3, 6, 9 pm)	Yes	[**Q3 FIFRA SAP 2007**]
Within Day Consumption of Direct DW: Bayer DW Consumption Survey	Yes	[**Q3 FIFRA SAP 2007**]
2-Diary	Yes	Similar to Method used in Agency risk assessments (e.g., Calendex-FCID™)
8-Diary	Yes	[**Q2 & Q5 FIFRA SAP 2007**; option available but not recommended; will be dropped in next update since data not included in NHANES]
Diary Assembly (DA)	Yes	Currently based on Total Caloric Intake
Residues (Food & Drinking Water)		
Commodity (FCID) Residues	Yes	Method used in OPP risk assessments (e.g., DEEM-FCID™)
Food Residue (vs. Commodity)	No	Option used to assess Arsenic (Journal article); Case study assigns residues to FCID commodities; Difficult to Incorporate in GUI
Drinking Water Concentrations	Yes	Single Distributions only (e.g., DEEM-FCID™)
Drinking Water Concentrations – Calendar Year	No	Randomly Select Year, then apply to corresponding Modeled Day (e.g., Calendex-FCID™ and CARES™ use of 30 years of PRZM-EXAMS predicted DW concentrations)
Modeling Food Residues		
Select Single Residue for all Eating Occasions, by Commodity (RAC-FF)	Yes	Method used in Agency risk assessments (e.g., DEEM-FCID™)
Select New Residue for different Eating Occasions, by Food-RAC-FF	Yes	[**Q1 FIFRA SAP 2007**, 32; Option often has little effect for food-only analyses; may 'add' uncertainty]
Correlation across commodities, across multiple chemicals (products) applied to foods, and	No	Minimal data to implement; (FIFRA SAP 2007, p.25)

DS-Dietary Option/Feature	Available in SHEDS-Dietary?	Notes [Option linked to 2007 FIFRA SAP Question]
over subsequent days		
Multiple Distributions for Commodity (RAC-FF)	No	E.g., probability of ‘Domestic’ or ‘Import’;
Multiple Distributions for Commodity (RAC-FF), By Season	No	[**Q5 FIFRA SAP 2007**] E.g., linking food consumption with seasonal (and/or regional) residues
Modeling Drinking Water Concentrations		
Randomly select new DW concentration each day	Yes	Method used in Agency risk assessments (e.g., DEEM-FCID™)
Randomly select Year for each Person-iteration, then apply Predicted DW based on Calendar (365) date	No	Retain seasonal patterns (autocorrelation) in DW concentrations. Method used in Agency risk assessments (e.g., Calendex-FCID™, CARES™)
Sensitivity/Uncertainty Analyses		
Sensitivity Analyses	*	Requires supplemental routine (e.g., effect of consumption outliers on infant DW exposures – aldicarb memo)
Uncertainty Analyses	*	[**Q4 FIFRA SAP 2007**] Requires supplemental routine
Compiling/Viewing Summary Statistics		
Total Daily Exposures (99.9th)	Yes	Measure used in OPP assessments
Average Daily Exposures (99.9th)	*	Need supplemental routine
Eating Occasions (99.9th) based on Maximum Exposure over all Eating Occasions	Yes	Method used to characterize exposures (NMC CRA)
Eating Occasions with Chemical-Specific Half-Life (99.9th)	*	Method used in DEEM-Based Eating Occasions analyses; Need supplemental routine. Supplemental program to calculate per capita 99.9th for single-chemical, single-day was recently incorporated into GUI; needs QC.
Plotting Person-Day Exposures	Yes	Visualize Exposure Patterns/Persisting Dose
Contribution Analyses: Shares of Total Exposure, by Commodity	Yes	Used to develop risk mitigation options
Contribution Analyses: Shares of Total Consumption, by Food (Commodity)	Yes	
Output Summary Results (99.9th, CEC, etc.) to File (MS Excel/MS Word)	*	SAS Editor/Wizard allow users to export results
View/Query Data (Food Diaries, Recipes, etc.)	*	SAS Editor allows users to view/query data
New Aggregate Contribution Analyses	*	Need supplemental routine

* not implemented in GUI but can be conducted using SAS code

1.2.1.1 Eating Occasion Analyses

In addition to providing estimates of total daily dietary exposure, SHEDS-Dietary provides the Agency with a capability to conduct 'Eating Occasions' analyses to refine risks for pesticides and other chemicals; such analyses have been discussed by several Panels (US EPA FIFRA SAP 1999, 2003, 2005). Research suggests that eating occasion analyses may refine the risk assessments for some compounds with short half-lives (U.S. EPA. 2007; Nako et al., 2007). Use of the Bayer Drinking Water Consumption Survey (DWCS) data in SHEDS-Dietary (and in the future, time of drinking water consumption data from NHANES) can be used to refine previous drinking water exposure analyses (e.g., revised OP CRA, NMC CRA; http://www.epa.gov/pesticides/cumulative/). Eating and drinking occasion algorithms in SHEDS-Dietary enhance the ability to model dietary exposures over short-term durations. Detailed information by eating occasion also allows conducting analyses to determine the contribution to exposure of different food types, chemicals, and other factors for different age-gender groups.

1.2.1.2 Half-life Analyses

SHEDS-Dietary v1 includes longitudinal algorithms to enhance the ability to model dietary exposures over short-term durations - less than a day, and up to one year, and to assess the impact of a chemical's half-life on the exposure results (e.g., "persisting effects" for organophosphates). For example, the SHEDS-Dietary longitudinal analyses can be used to assess exposure bio-indicators persisting across multiple exposure events (e.g., on cholinesterase inhibition for organophosphates). By including recovery half-lives, fraction of the peak effect persisting from one exposure event is considered when a second exposure event occurs later.

1.2.1.3 Uses CSFII or NHANES/WWEIA Food Consumption Data

SHEDS-Dietary can use the USDA's CSFII 1994-96, 1998 or the NHANES/WWEIA 1999-2006 food consumption data. The 1994-1996, 1998 CSFII data base included 5,845 food items consumed by respondents. The NHANES respondents reported consuming many of those same foods, as well as approximately 580 new foods that were not reported during the CSFII survey. As part of the transition to using the newer NHANES data, the Office of Pesticide Programs is currently planning to update the food recipe data base (FCID) to include new foods that were not reported by respondents in the CSFII survey. Approximately 20g (or approximately 1% of all food eaten by individuals) of new NHANES foods are not matched to CSFII foods (see Appendix F); however, our analyses have shown this does not affect results. Using this Agency model provides OPP a quick and economical means to assess the National Health and Nutrition Examination Survey (NHANES) food consumption data for modeling dietary exposures.

1.2.1.4 Options for Simulating Longitudinal Consumption Data

While the main focus to date in SHEDS-Dietary has been on the cross-sectional algorithms, the model is capable of modeling longitudinal dietary exposures to chemicals. For this purpose, SHEDS-Dietary requires the construction of human consumption diaries that cover the entire simulation period of a model run. This period is often several months, a year, or even longer. For a simulated individual, SHEDS-Dietary constructs a longitudinal profile of food consumption over a 365 day period with 3 options: a cross-sectional or 2-diary approach; an 8-

diary approach, and the "D&A" approach (Glen et al., 2007) described below. Issues relating to longitudinal diary construction are described later in this manual.

In both CSFII and NHANES, there are two-day dietary consumption data for the subjects. Therefore, we can use two-day data for the same person together with many run interactions to assemble the longitudinal data. For example, the residues are randomly assigned to one person with two-day dietary consumption data, which is counted as one interaction. The same two-day data will be randomly assigned with different residue concentrations. This is another interaction. In this way, many interactions can be generated. Then, data from the first interaction will be counted as day 1 and 2, the second as day 3 and 4 and so on. In this way, longitudinal data will be assembled.

The 8-diary longitudinal algorithm (Xue et al., 2004) is the same approach used in the SHEDS-Multimedia model, which constructs longitudinal activity profiles from human activity diaries drawn from EPA's CHAD (Consolidated Human Activity Database; McCurdy et al., 2000; http://www.epa.gov/chadnet1). CHAD typically includes just one day (24 hours) of activities from each person. SHEDS-Dietary creates modeled individuals (reference population) by randomly drawing a person from the Census data. The food consumption diaries used by SHEDS-Dietary (NHANES or CSFII; see later sections) are grouped by age and gender, and for each of these age-gender cohorts, 'diary pools' are created based on Season and Day of Week (weekday or weekend). For each modeled individual, SHEDS-Dietary constructs a longitudinal profile of food consumption by randomly selecting 8 food diaries (one weekend and one weekday, for each of the four seasons) from the appropriate cohort-diary pools. NHANES/WWEIA does not provide dates, so SHEDS-Dietary randomly draws consumption diaries from that survey to use this approach.

The August 2007 FIFRA SAP reviewed this approach for dietary exposure assessment, and found 8 diaries to be insufficient. Thus, a more detailed and desirable option for assembling year-long diaries is given in Glen et al., 2007. The user chooses target behavior and statistics to control within- and between- person variance, and day-to-day autocorrelation. Diaries are preferentially sampled to produce the target behavior. This method, referred to as the "D&A approach", requires a few additional inputs to be designated by the user, but allows for more control over the properties of the assembled diaries. This diary assembly method requires the user to:

1) select the diary property most relevant to exposure for the current application (e.g., Total Calories);
2) specify the "D" (diversity) statistic, which relates the within-person and between-person variances for this diary property; and
3) specify the 1-day lag autocorrelation "A" in this diary property.

Guideline values for the D and A statistics for a number of diary properties have been calculated using the steps below for the permethrin case study, but other values can be used as more data become available:

1) Calculate the total amount of major vegetables contributing to dietary permethrin exposure. Those vegetables are spinach, cabbage, lettuce, parsley, celery and tomato.

2) Use the total amount of those vegetables consumption (grams) per day as index to calculate D and A statistics.
3) Results: D=0.27 and A=0.06
4) Total calories consumption was used with 0.3 for D and 0.1 for A statistics, based on data from Lu et al. (2006a,b) (Alex Lu, personal communication), to assemble the longitudinal diary for one year.

1.2.1.5 Multi-chemical (Cumulative Exposure Assessment) Capability

There are two key differences between the single chemical and cumulative exposures in the SHEDS-Dietary model: 1) co-occurrence of the chemicals; and 2) addition of exposures among chemicals with similar mode of action. Different SAS code modules in the model are used to accommodate these differences even though they share a common algorithm. For pesticides, there is a small data set storing pesticide codes, usually in three letters or digits. Selected pesticides (pesticide codes) will be used to merge the residue data. Due to co-occurrence, pesticides measured in the same raw agricultural commodity (RAC) or food item will be stored in the same place labeled by the same identifier so that it will be selected as whole by Monte Carlo simulation. For adding exposures to obtain cumulative exposure, relative potency factors are used so that exposures of different pesticides can be added, weighted by the relative toxicities.

1.2.1.6 Linkage to PBPK Models

The timing of exposures throughout a simulated day becomes important as the Agency moves toward integrating dietary exposure models with physiologically-based pharmacokinetic models. To account for eating occasions, SHEDS-Dietary preserves information from the detailed food diaries and corresponding exposure calculations. Linkage between SHEDS-Dietary exposure outputs, which preserve variability of exposures within a day, and physiologically-based pharmacokinetic (PBPK) models allows for refined dose and risk analyses, and evaluation of SHEDS-Dietary model performance against NHANES biomonitoring data (Xue et al., 2010).

1.2.1.7 Sensitivity and Uncertainty Analyses

SHEDS modeling research has involved developing and applying new methods for sensitivity and uncertainty analyses (Xue et al., 2006; Zartarian et al., 2007; http://www.epa.gov/heasd/products/sheds_multimedia/sheds_mm.html; http://www.epa.gov/scipoly/SAP/meetings/2007/081407_mtg.htm). These methods can be applied to different model applications for identifying key factors, outliers, and data needs.

1.2.2 Plans and Future Research Needs

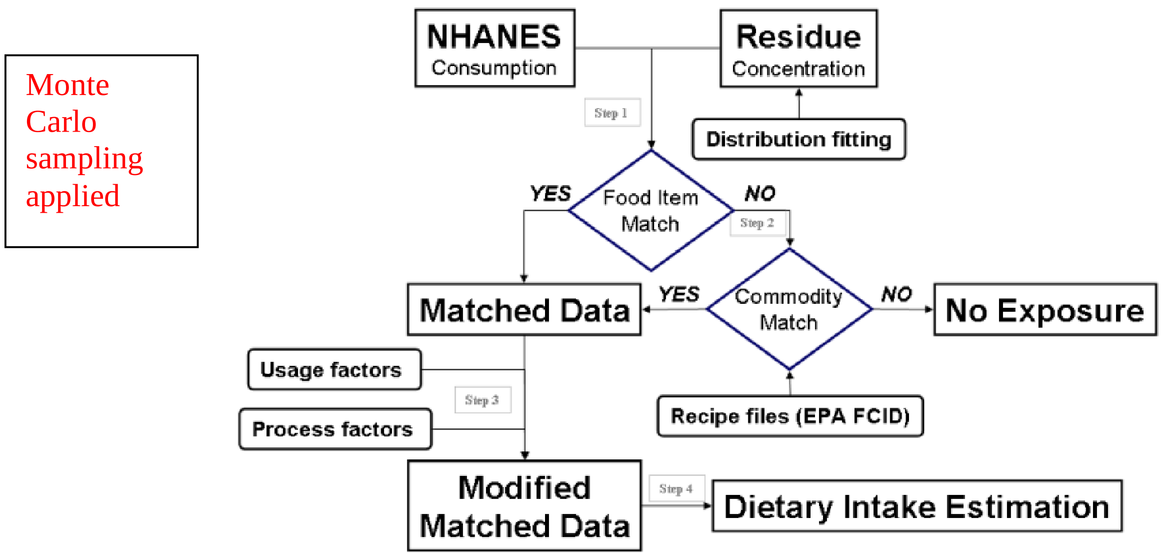
Plans and future research needs for SHEDS-Dietary include the following:

- Apply to other case studies with PBPK linkage, sensitivity and uncertainty analyses, model evaluation;
- Expand model applications to local/community scale for different chemicals;
- Refine longitudinal algorithms based on available data;
- Merge dietary & residential modules (match food consumption and activity diaries);

- Analyze impact of different residue sampling: same vs. different residues within a day for same foods eaten by an individual;
- Possible refinements to drinking water allocations;
- Explore enhancements to uncertainty analyses;
- Expand the model to local scale applications for different chemicals, seasons, regions; methods (including analyses of CSFII and NHANES) to examine importance of region- and season- specific dietary consumption amounts and patterns on dietary exposure estimates;
- Consider other data sets for considering enhancing within-day modeling of exposures e.g. Child Development Supplement to Panel Study of Income Dynamics (http://psidonline.isr.umich.edu/CDS/time_diary_readme.html), American Time Use Survey (ATUS), http://www.bls.gov/tus/#overview, University of Maryland archive on recent and historical data sets on individual time use and activity patterns, http://www.webuse.umd.edu); and
- Conduct more research on sampling drinking water concentrations (e.g., randomly select a year then apply daily concentrations throughout the modeled calendar year).

2 SHEDS-Dietary Methodology

The SHEDS-Dietary Module overview is illustrated in Figure 2-1, and details on the algorithms are given in the following sections and the annotated code in Appendix G.



NHANES Consumption: Food consumption data from NHANES
Residue Concentration: Residue concentration data by food item or commodity from TDS
Distribution fitting: fittings of residue data into suitable statistical distribution
Food Item: food products people in the survey consumed such pizza, raw apple
Commodity: raw agriculture commodity (RAC)
Usage factors: Pesticide usage percentages by RAC from USDA.
Process factors: concentration or dilution factors due to processes of food from RAC into food products.
Recipe files (EPA FCID): data base for percents of various RACs for the food products.

Figure 2-1. SHEDS-Dietary Methodology (modified from Xue et al. 2010)

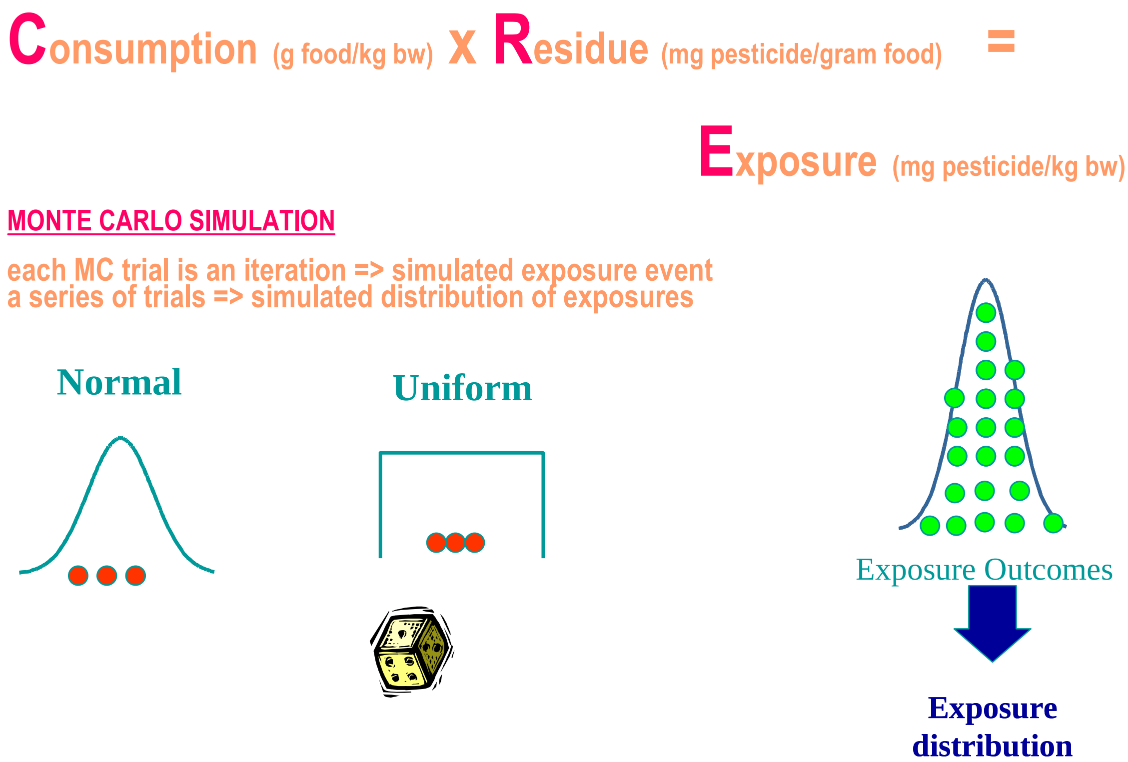


Figure 2-2. Monte Carlo Simulation in Dietary Exposure Modeling

Xue et al., 2010 describes the SHEDS-Dietary methodology shown in Figure 2-1. For estimating daily dietary exposure, detailed NHANES (or CSFII) food diaries are used by the SHEDS-Dietary model to simulate food ingestion exposures by separate eating occasions for a simulated individual (Figure 2-1). SHEDS-Dietary can use residues for food items as consumed, as well as residues of raw agricultural commodities (RAC). The reported food items are matched with food items in the FDA's Total Diet Study (TDS) where possible (see step 1 in Figure 2-1). If TDS residues are available for a particular food (e.g., rice, chicken), then SHEDS-Dietary randomly draws a TDS residue from that corresponding residue distribution of the same food. Otherwise, the model applies the FCID recipe files to the NHANES or CSFII food items and randomly selects a residue for each of the RAC ingredients according to the recipe (see step 2 in Figure 2-1). Note that SHEDS-Dietary version 1 does not implement the option of sampling residues from food items as consumed, e.g., TDS.

Through the recipe files, the unmatched foods consumed are matched by RAC so that residues for those foods can be calculated. One option in SHEDS-Dietary version 1 for sampling residues within a day is to draw the same residue value if that RAC is found in the same foods. A second option is to draw different residue values for the same foods within a day. For non-detects, the model can assign zero or ½ LOD, depending on the chemical usage information (see details below). For each NHANES food diary, SHEDS-Dietary selects a residue value from an empirical distribution for each TDS food or RAC. While a particular commodity may be used in multiple foods, the cooking method may differ, and thus, it will have a different food form. Process factors can then be applied (see step 3 in Figure 2-1). These factors account for food changes and related concentration changes due to dilution, drying, etc.. Each simulated individual's exposure for each commodity is calculated by multiplying eating occasion consumption with corresponding residues. Summation of exposures from every eating occasion for one day yields the individual's total daily exposure (see step 4 in Figure 2-1). Monte Carlo simulation is applied to generate population estimates of dietary exposure (see Figure 2-2). More details on the food and drinking water ingestion exposure algorithms are given below.

2.1 Algorithm for Estimating Exposure to Pesticides and Other Toxicants from Food Consumption

SHEDS-Dietary v1 incorporates the data and decisions illustrated in Figure 2-1 above, and calculations shown in Equations 1 and 2 below, to calculate food ingestion exposure. The model uses food consumption diaries to simulate individuals' food ingestion exposures by separate eating occasions. Reported consumption data are combined with sampled chemical residues in foods consumed, and concentration or dilution factors that adjust the residues for changes due to food processing (Figure 2-1). This section briefly introduces the equations used for calculating dietary exposure and their inputs, which are detailed in subsequent sections.

Total daily exposure is calculated by summing exposures across all commodities, as depicted in Equation (1). Each simulated individual's exposure for each commodity is calculated by multiplying the eating occasion consumption with the corresponding residues and process factors:

Equation (1) – SHEDS-Dietary Equation for Estimating an Individual's Exposure from a Single Eating Occasion

Individual's Dietary Exposure for a Single Eating Occasion [mass chemical] = amount of food item consumed [mass food] x concentration in the food item [mass chemical/ mass food] x process factors

Equation (2) – SHEDS-Dietary Equation for Estimating an Individual's Total Daily Exposure from All Eating Occasions

Individual's Total Daily Exposure = Σ(Individual's Dietary Exposure for a Single Eating Occasion) over all eating occasions in a given day.

Population estimates are obtained by applying Monte Carlo simulation as shown in Figure 2-2; the algorithms for computing an individual's total daily exposure are repeated thousands of times to obtain a population cumulative density function (CDF).

2.1.1 Consumption

The food consumption diaries used by SHEDS-Dietary and other dietary exposure models (such as those shown in Table 2-1) contain information on the timing and amounts consumed as reported by the survey respondents. Note that food and water consumption quantities are recorded in units of ounces, cups, or by count (cf. Egg, whole, Table 2-1). These units are converted to grams and ml for calculations. Appendix A contains details on food consumption data used in SHEDS-Dietary version 1.

Table 2-1. An Example CSFII Food Diary (CSFII ID=28517-2-2: 1 yr, M, 13.6 kg).

SEQN	Time of Day	Food Description	Amount (unit code)	Consumption (gm)	Food Source /1
1	7:00 AM	Milk, cow's, fluid, whole	6 fl.oz (10205)	183	Store
2	10:15 AM	Egg, whole, fried W/ LARD	2 XX (60919)	92	Store
3		White potato, home fries W/ LARD	2 C (10205)	388	Store
4	6:00 PM	Chicken, drumstick, with or without bone, roasted, skin eaten	1 XX (61343)	52	Store
5		White potato, home fries W/ LARD	2 C (10205)	388	Store
6	8:00 PM	Milk, cow's, fluid, whole	6 fl.oz (10205)	183	Store

/1 The Food Source variable is based on the question, 'Where was the food item obtained?' (1=store, etc.).

2.1.2 Residues and Process Factors

In principle, food residues as well as drinking water concentrations may also vary by eating occasion and/or foods consumed throughout the day. With that modeling assumption, the SHEDS-Dietary eating occasion approach tracks exposures throughout the simulated day based on the food diary data. Currently in SHEDS-Dietary, the user has 2 options for sampling residues consumed by an individual on multiple eating occasions within a day: (1) same residue sampled for same RAC and food items within a given day; (2) different residues sampled for all RAC and food items within in a given day.

In SHEDS-Dietary version 1.0, empirical distributions are be used for raw agricultural commodities (RAC; see Appendix C). Reported food items are matched with food items (e.g., 2% milk, raw apple) in the Total Diet Study (TDS; http://www.fda.gov/Food/FoodSafety/FoodContaminantsAdulteration/TotalDietStudy/default.htm) where possible; the model randomly draws a residue from that corresponding TDS residue distribution of same food. For unmatched foods, the model applies FCID recipe files to the food items and randomly selects a residue for each of the RAC ingredients according to the recipe so that residues for those foods can be calculated (this approach is used for pesticides).

The current version of SHEDS-Dietary does not include the option of matching reported foods (note that modifications were conducted for the arsenic case study to allow food items as consumed as depicted in Figure 2-1) where possible with foods reported "as eaten" (e.g., pizza rather than the pizza RAC tomatoes, flour, etc.) (e.g., in the FDA in the TDS), so that residues for those foods can be sampled; the model randomly draws a residue from that corresponding food residue distribution. A particular commodity may be used in multiple foods, with different cooking methods; thus, it will have a different food form reported. Process factors can be applied that account for food changes and related concentration changes due to dilution, drying, etc. Through recipe files (see Appendix E), unmatched foods consumed are matched by RAC so that residues for those foods can be calculated. SHEDS-Dietary randomly selects a residue from the corresponding RAC-food form distributions for those unmatched foods, according to the recipe amounts of those RAC. The exposure from each commodity-food form (RAC-FF) is calculated by multiplying that residue value with the amount consumed.

Assignment of RAC residues for non-detects depends on the percent detected in PDP for the commodity and the percent of crops using that chemical. For example, if 20% of a crop is treated with Chemical X, and 5% of samples in PDP had detectable residues, then SHEDS-Dietary used the actual values for the 5%, assumes ½ LOD for 15%, and 0 for 80%. If the crop is not treated with Chemical X, the LOD is assigned zero.

2.1.3 Sample calculation

Total daily exposure is calculated in SHEDS-Dietary by summing chemical exposures across all commodities. Summation of chemical exposures from every commodity and every eating occasion for one day yields the individual's daily total dietary exposure.

This equivalence is illustrated with the following simple numerical example using the diary from a 1 yr old child (Table 2-1; CSFII ID=28517-2-2). If we assume that 47 grams of potatoes was consumed at 10:15 am from food, "White potato, home fries W/ LARD" and a residue of 1 ppm was drawn only for 'potatoes', then the exposure is 0.047 mg for this eating occasion. At 6:00 pm, the same amount of the same food was consumed, therefore, 1 ppm of residue for the potato was used again due to the same food, then exposure for this eating occasion is also 0.047 mg: Exposure = 47 gms x (1/1000) x 1 (mg/kg) = 0.047 mg.

If exposure from egg was 0.05 mg and that was the only other food to contribute any exposure that particular day, then total daily exposure for the subject will be the summation of 0.047,0.047 and 0.05, i.e. 1.44 mg/day. Options for modeling food residues (i.e., randomly drawing different residues) are discussed in a subsequent section. A model specification could select a new residue for the same RAC-FF consumed through different foods (e.g., milk versus other dairy products).

This process is repeated for many simulated individuals (for each food consumption diary, or simulated person-day) via Monte Carlo sampling (see Figure 2-2) to generate population estimates of dietary exposure (Xue et al., 2010). For any particular diary, a Monte Carlo simulation is performed to select a residue concentration for each food commodity (raw agricultural commodity – food form; RAC-FF).

2.2 Drinking Water Exposure Algorithm

The SHEDS-Dietary drinking water exposure algorithm is similar to that for food exposure. Because the CSFII data does not provide information on timing and amounts of direct water intake throughout the day, SHEDS-Dietary currently distributes total direct water consumption from this database in 6 equal amounts at 6 fixed times (6am, 9am, 12pm, 3pm, 6pm, 9pm). The more recent NHANES 2005-2006 did collect information on timing and amounts of direct water intake throughout the day, so that information can also be used directly in SHEDS-Dietary in the future to assess timing and amounts of direct drinking water (e.g., tap, bottled) and indirect drinking water (e.g., infant formula, 'kool aid', coffee, tea, water used in cooking) intake within a simulated person-day (see Appendix A). Total drinking water consumed (both direct and indirect water consumption) is assumed to contain the same concentration, i.e., only one concentration value is selected in the Monte Carlo simulation for each eating occasion. SHEDS-Dietary randomly draws a drinking water concentration for each person-day (similar to DEEM-FCID). One residue value is randomly selected and multiplied by total water intake to obtain drinking water exposures. In principle, drinking water concentrations may vary based on source (e.g., tap, bottled, other source); this is an area of future research. Currently, SHEDS-Dietary randomly draws drinking water concentration for any given day (no seasonality).

2.3 Inputs

This section summarizes the data used by SHEDS-Dietary to assess dietary exposures.

2.3.1 Food and Indirect Water Consumption Data

The primary sources of consumption data used in SHEDS-Dietary to model dietary exposures to pesticides are the food consumption diaries in the U.S. Department of Agriculture's Continuing Survey of Food Intakes by Individuals (CSFII) database and in the NHANES/What We Eat in America (WWEIA) 1999-2006 database (see Appendices A, C, D, E). These surveys contain information regarding the real-time reported amount of food and water consumed by individuals, i.e. amounts of food and drinking water reported by individuals for each separate eating occasion.

The CSFII food diaries contain information collected through a multiple pass 24-hour dietary recall instrument that was administered by trained interviewers in the respondents' homes (Day 1) or by phone interview (Day 2). Individuals were asked to provide food intake on 2 nonconsecutive days (3 to 10 days apart) as well as socioeconomic and health-related information. A total of 20,607 individuals provided two 24 hour food diaries (total of 41,214 diaries) during the initial survey period, 1994-1996, and through a children's supplemental survey conducted in 1998 to address FQPA requirements that the USDA provide food intake data for a statistically adequate sample of children for use by the EPA to estimate exposure to pesticide residues. Table 2-2 shows an example diary from CSFII.

The NHANES/WWEIA 1999-2006 food consumption data (53,522 diaries) are also 24 hour recalls. The first day (Day 1) diary was collected through in-person interviews in the Mobile Examination Centers (MEC), while the second day 24 hour recall diary is collected by telephone, approximately 10 days after the in-person interview.

Table 2-2. Example CSFII Food Consumption Diary

Example of food consumption data for HHID=11328 and SPNUM=2 for two days
(Female and 1 years old)

DAYCODE	OCC_TIME	foodname	FOODAMT (grams)
1	800	MILK, COW'S, FLUID, 1% FAT	183
1	800	APPLE JUICE, W/ ADDED VITAMIN C	186
1	800	APPLE, RAW	138
1	800	CHEERIOS	30
1	800	MILK, COW'S, FLUID, 1% FAT	122
1	930	CRACKERS, CHEESE	124
1	1230	WHITE POTATO, CHIPS (INCL FLAVORED)	40.5
1	1230	PEPPER, SWEET, RED, RAW	74.5
1	1230	PEAR, RAW	166
1	1230	APPLE, RAW	69
1	1230	MILK, COW'S, FLUID, 1% FAT	122
1	1230	BREAD, POTATO	52
1	1230	TUNA SALAD	26
1	1530	APPLE JUICE, W/ ADDED VITAMIN C	186
1	1830	RICE, FRIED, W/ MEAT/POULTRY	198
1	1830	PORK, SPARERIBS, COOKED, LEAN ONLY	72
1	1830	CHICKEN PATTY/FILLET/TENDERS, BREADED, COOKED	176
1	1830	MILK, COW'S, FLUID, 1% FAT	122
1	1830	CRANBERRY JUICE DRINK W/VIT C ADDED(INCL COCKTAIL)	126.5
1	1900	ICE CREAM, REGULAR, NOT CHOCOLATE	44
2	800	MILK, COW'S, FLUID, 1% FAT	122
2	800	TEA, MADE FROM POWDERED INSTANT, PRESWEETENED	118.4
2	800	CHEERIOS	37.5
2	800	MILK, COW'S, FLUID, 1% FAT	183
2	1000	PUFFED RICE CAKE	9
2	1000	TEA, MADE FROM POWDERED INSTANT, PRESWEETENED	118.4
2	1200	CHICKEN VEGETABLE SOUP,W/RICE,MEXICAN(SOPA / CALDO DE POLLO)	242
2	1200	BREAD, ITALIAN, GRECIAN, ARMENIAN	20
2	1200	MILK, COW'S, FLUID, 1% FAT	122
2	1500	APPLE, RAW	138
2	1830	CORN DOG (FRANKFURTER/HOT DOG W/ CORNBREAD COATING)	88
2	1830	MILK, COW'S, FLUID, 1% FAT	122
2	1830	COUSCOUS, PLAIN, COOKED, FAT ADDED IN COOKING	81
2	1830	PORK & VEG (W/ CAR/DK GREEN, NO POTATO), NO SAUCE	81

2.3.2 Recipe Files

For the purpose of assessing food tolerance, the EPA developed the Food Commodity Intake Database (FCID) that converts CSFII food items (e.g., apple pie, hamburger, milk and other diary products) into Raw Agricultural Commodities (RAC) based on likely cooking method and food form (FF) (Appendix E). The FCID database contains recipes or each food item reported in the 1994-1996, 1998 CSFII diaries. These recipes (see Table 2-3) allow the model to calculate contributions from each food (e.g., pork and vegetables, fried rice) to aggregate exposures. FCID recipe files break down foods into 553 RAC. Recipes are being developed by OPP for new NHANES/WWEIA food items (anticipated release, Fall 2010).

The FCID commodity diaries may underestimate dietary exposures from some food items. For example, the FCID recipe decomposes an 8 oz. glass of whole milk (244 g) into three components: water (88%), fat (3.3%), and non-fat solids (8.7%). A simulation based on the food recipes entails randomly selecting a residue for each of the three components, and calculating contributions based on the corresponding weights: 214 g, 9 g, and 21 g, respectively. The assumption that residues are independent may lead to underestimating exposures to the extent that some components (e.g., water and fat) contain residues (treated), while the other components (non-fat solids) do not. Ideally, the user may want to directly apply the PDP data, because milk samples, collected from distribution centers and supermarkets, reflect foods as consumed by persons, and thus, do not require additional modeling assumptions regarding correlations (independence) across the components. The advantage of the FCID commodity diaries is that it facilitates developing anticipated residues for hundreds of other diary products, since the recipes account for different contributions from water, fat, and non-fat solids. SHEDS-Dietary version 2 will allow the user to specify residues for both foods as eaten and/or commodities - as applied in Xue et al., 2010.

Table 2-3. Example Recipe File for Two Food Items

Food Items	RAC	CM_name	CS_name	FF_name	Percent
PORK & VEG (W/ CAR/DK GREEN, NO POTATO), NO SAUCE	Bean, lima, succulent	Not specified	Cooked	Fresh or N/S	3.96
	Bean, snap, succulent	Not specified	Cooked	Fresh or N/S	10.45
	Carrot	Not specified	Cooked	Fresh or N/S	15.84
	Corn, sweet	Not specified	Cooked	Fresh or N/S	15.84
	Pea, succulent	Not specified	Cooked	Fresh or N/S	10.45
	Pork, fat	Not specified	Cooked	Fresh or N/S	5.995
	Pork, meat	Not specified	Cooked	Fresh or N/S	37.127
'RICE, FRIED, W/ MEAT/POULTRY	Bean, mung, seed	Fried	Cooked	Fresh or N/S	0.486
	Chicken, fat	Fried	Cooked	Fresh or N/S	0.504
	Chicken, meat	Fried	Cooked	Fresh or N/S	6.285
	Corn, field, oil	Not specified	Refined	Not Applicable	0.201
	Cottonseed, oil	Not specified	Refined	Not Applicable	0.319
	Egg, whole	Fried	Cooked	Fresh or N/S	10.741
	Olive, oil	Not specified	Refined	Not Applicable	0.082
	Onion, green	Fried	Cooked	Fresh or N/S	2.8
	Pea, succulent	Fried	Cooked	Fresh or N/S	3.42
	Peanut, oil	Not specified	Refined	Not Applicable	0.055
	Rapeseed, oil	Not specified	Refined	Not Applicable	0.169
	Rice, white	Fried	Cooked	Fresh or N/S	24.24
	Safflower, oil	Not specified	Refined	Not Applicable	0.001
	Sesame, oil	Not specified	Refined	Not Applicable	0.001
	Soybean, oil	Not specified	Refined	Not Applicable	3.556
	Soybean, seed	Fried	Cooked	Fresh or N/S	0.956
	Sunflower, oil	Not specified	Refined	Not Applicable	0.007
	Water, indirect, all sources	Fried	Cooked	Fresh or N/S	39.31
	Wheat, flour	Fried	Cooked	Fresh or N/S	0.376

Table 2-4. Example CSFII Food Consumption Data for Two Days

Example of food consumption data for HHID=11328 and SPNUM=2 for two days
(Female and 1 years old)

DAYCODE	OCC	TIME	foodname	RAC	CM_name	CS_name	FF_name	amount_gram
1		800	MILK, COW'S, FLUID, 1% FAT	Milk, fat	Not specified	Uncooked	Fresh or N/S	1.94
1		800	MILK, COW'S, FLUID, 1% FAT	Milk, nonfat solids	Not specified	Uncooked	Fresh or N/S	16.21
1		800	MILK, COW'S, FLUID, 1% FAT	Milk, water	Not specified	Uncooked	Fresh or N/S	164.85
1		800	APPLE JUICE, W/ ADDED VITAMIN C	Apple, juice	Not specified	Uncooked	Fresh or N/S	185.93
1		800	APPLE, RAW	Apple, fruit with peel	Not specified	Uncooked	Fresh or N/S	138.00
1		800	CHEERIOS	Beet, sugar	Not specified	Refined	Not Applicable	0.40
1		800	CHEERIOS	Cassava	Not specified	Cooked	Dried	0.01
1		800	CHEERIOS	Corn, field, starch	Not specified	Cooked	Dried	0.93
1		800	CHEERIOS	Oat, groats/rolled oats	Not specified	Cooked	Dried	29.94
1		800	CHEERIOS	Potato, flour	Not specified	Cooked	Dried	0.01
1		800	CHEERIOS	Rice, flour	Not specified	Cooked	Dried	0.01
1		800	CHEERIOS	Sugarcane, sugar	Not specified	Refined	Not Applicable	0.51
1		800	CHEERIOS	Wheat, flour	Not specified	Cooked	Dried	0.01
1		800	MILK, COW'S, FLUID, 1% FAT	Milk, fat	Not specified	Uncooked	Fresh or N/S	1.29
1		800	MILK, COW'S, FLUID, 1% FAT	Milk, nonfat solids	Not specified	Uncooked	Fresh or N/S	10.81
1		800	MILK, COW'S, FLUID, 1% FAT	Milk, water	Not specified	Uncooked	Fresh or N/S	109.90
1		930	CRACKERS, CHEESE	Barley, flour	Baked	Cooked	Fresh or N/S	0.45
1		930	CRACKERS, CHEESE	Cottonseed, oil	Not specified	Refined	Not Applicable	2.08
1		930	CRACKERS, CHEESE	Milk, fat	Baked	Cooked	Fresh or N/S	4.49
1		930	CRACKERS, CHEESE	Milk, nonfat solids	Baked	Cooked	Fresh or N/S	4.08
1		930	CRACKERS, CHEESE	Milk, water	Baked	Cooked	Fresh or N/S	1.15
1		930	CRACKERS, CHEESE	Pepper, nonbell, dried	Baked	Cooked	Fresh or N/S	0.27
1		930	CRACKERS, CHEESE	Soybean, oil	Not specified	Refined	Not Applicable	23.91
1		930	CRACKERS, CHEESE	Wheat, flour	Baked	Cooked	Fresh or N/S	92.66
1		1230	WHITE POTATO, CHIPS (INCL FLAVORED)	Corn, field, oil	Not specified	Refined	Not Applicable	1.30
1		1230	WHITE POTATO, CHIPS (INCL FLAVORED)	Cottonseed, oil	Not specified	Refined	Not Applicable	0.97
1		1230	WHITE POTATO, CHIPS (INCL FLAVORED)	Potato, chips	Fried	Cooked	Fresh or N/S	26.14
1		1230	WHITE POTATO, CHIPS (INCL FLAVORED)	Rapeseed, oil	Not specified	Refined	Not Applicable	0.54
1		1230	WHITE POTATO, CHIPS (INCL FLAVORED)	Safflower, oil	Not specified	Refined	Not Applicable	0.00
1		1230	WHITE POTATO, CHIPS (INCL FLAVORED)	Soybean, oil	Not specified	Refined	Not Applicable	11.02
1		1230	WHITE POTATO, CHIPS (INCL FLAVORED)	Sunflower, oil	Not specified	Refined	Not Applicable	0.04
1		1230	PEPPER, SWEET, RED, RAW	Pepper, bell	Not specified	Uncooked	Fresh or N/S	74.50
1		1230	PEAR, RAW	Pear	Not specified	Uncooked	Fresh or N/S	166.00
1		1230	APPLE, RAW	Apple, fruit with peel	Not specified	Uncooked	Fresh or N/S	69.00
1		1230	MILK, COW'S, FLUID, 1% FAT	Milk, fat	Not specified	Uncooked	Fresh or N/S	1.29
1		1230	MILK, COW'S, FLUID, 1% FAT	Milk, nonfat solids	Not specified	Uncooked	Fresh or N/S	10.81
1		1230	MILK, COW'S, FLUID, 1% FAT	Milk, water	Not specified	Uncooked	Fresh or N/S	109.90
1		1230	BREAD, POTATO	Beet, sugar	Not specified	Refined	Not Applicable	1.29
1		1230	BREAD, POTATO	Cottonseed, oil	Not specified	Refined	Not Applicable	0.13
1		1230	BREAD, POTATO	Guar, seed	Baked	Cooked	Fresh or N/S	0.06
1		1230	BREAD, POTATO	Milk, fat	Baked	Cooked	Fresh or N/S	0.49
1		1230	BREAD, POTATO	Milk, nonfat solids	Baked	Cooked	Fresh or N/S	2.27
1		1230	BREAD, POTATO	Milk, water	Baked	Cooked	Fresh or N/S	0.17
1		1230	BREAD, POTATO	Potato, flour	Baked	Cooked	Fresh or N/S	1.17
1		1230	BREAD, POTATO	Soybean, flour	Baked	Cooked	Fresh or N/S	0.29
1		1230	BREAD, POTATO	Soybean, oil	Not specified	Refined	Not Applicable	1.50
1		1230	BREAD, POTATO	Sugarcane, sugar	Not specified	Refined	Not Applicable	1.64
1		1230	BREAD, POTATO	Wheat, flour	Baked	Cooked	Fresh or N/S	33.30
1		1230	TUNA SALAD	Beet, sugar	Not specified	Refined	Not Applicable	0.02
1		1230	TUNA SALAD	Celery	Not specified	Uncooked	Fresh or N/S	1.90
1		1230	TUNA SALAD	Coriander, leaves	Not specified	Cooked	Canned	0.01
1		1230	TUNA SALAD	Coriander, seed	Not specified	Cooked	Canned	0.01
1		1230	TUNA SALAD	Corn, field, syrup	Not specified	Cooked	Canned	1.68
1		1230	TUNA SALAD	Cucumber	Not specified	Cooked	Canned	2.00
1		1230	TUNA SALAD	Egg, whole	Not specified	Cooked	Canned	0.16
1		1230	TUNA SALAD	Egg, yolk	Not specified	Cooked	Canned	0.11
1		1230	TUNA SALAD	Fish-saltwater finfish, tuna	Not specified	Cooked	Canned	14.08
1		1230	TUNA SALAD	Ginger, dried	Not specified	Cooked	Canned	0.01
1		1230	TUNA SALAD	Herbs, other	Not specified	Cooked	Canned	0.01
1		1230	TUNA SALAD	Lemon, juice	Not specified	Cooked	Canned	0.05
1		1230	TUNA SALAD	Onion, dry bulb	Not specified	Uncooked	Fresh or N/S	2.54

Table 2-2 provides an example of real dietary consumption data for one person over two days. Table 2-3 shows an example recipe files for two food items consumed by the subjects (there are many other food items in the recipe files not shown). Through recipe files, consumption data in Table 2-2 can be converted into the format in Table 2-4, so that the exact amount of RAC consumed by the subject will be used to be assigned with residue concentrations by RAC.

2.3.3 Direct Water Consumption Data

As discussed above, SHEDS-Dietary version 1 distributes total direct water consumption from the CSFII database in 6 equal amounts at 6 fixed times (6am, 9am, 12pm, 3pm, 6pm, 9pm). The more recent NHANES 2005-2006 did collect information on timing and amounts of direct water intake throughout the day, so that information can also be used directly in SHEDS-Dietary in future versions.

Another option for drinking water consumption data in SHEDS-Dietary is available. For any modeled individual, a drinking water diary is randomly selected from the Bayer DWCS data based on similar socioeconomic characteristics (age, gender, season). Bayer CropScience sponsored a study on direct drinking water consumption entitled "Drinking Water Consumption Survey" (DWCS), to evaluate this issue (Barraj et.al. 2004). The objective of this study was to obtain a distribution of water intake for a 24-hour time period that was nationally representative sample of the US population. The DWCS was conducted in two waves, in August 2000 (wave 1=- summer), and March 2001 (wave 2 = winter). The report provides the following description on the study design (Barraj et.al. 2004, pp.9-10):

> *"The National Product Database group (NPD) was chosen to conduct this survey because of its experience in tracking the consumption habits of the US population since 1980 through its National Eating Trends (NET®) service (NET®, 2004)." "Two nationally representative samples (one for each wave) were extracted from a core sample of 250,000 households from NPD's Home Testing Institute (HTI) consumer panel. The sample for wave 1 included 3,000 households randomly selected from the core sample of 250,000 households, while in an effort to increase the number of children in the survey, the sample for wave 2 included 650 households randomly selected from households with children less than 6 years of age in addition to 3,000 households randomly selected from the core sample." "One thousand nine hundred ninety-two participants in 994 households (33% response rate) completed the first wave of the survey, and 2,950 participants in 1,320 households (36% response rate) completed the second wave of the survey."*

Participants recorded their water consumption (time of day and amount consumed) over a one-week (7 day) period. The following information was collected in the DWCS diaries:

- Date and day of the week;
- Age and gender of the household member;
- Source of the home's drinking water (municipal, well);
- Time period of water consumption episode (18 hourly intervals starting at 6 am, and one 6 hr interval corresponding to the midnight-6 am period);

- Number of ounces of water consumed per time period (in 2-ounce bins);
- Where the consumption episode occurred (home/work or school/other);
- Whether the water was consumed with a meal; and
- The type of water consumed (tap/bottled).

A number of diaries were not used due to incomplete or missing information. The resulting database contained data from 4,198 individuals from 2,154 households, providing a total of 27,282 person-day diaries (approximately 83% of the total of all participants returned diaries for all 7 days).

Pesticide Use (% crop treated)
The pesticide use information, in particular the percent of crop treated (PCT) with a particular chemical, is used to determine how many samples were not treated and may be assumed to have no residues (true zero). This variable may come from either the USDA National Agricultural Statistics Service or proprietary data.

2.3.4 Process Factors

"Process factors" include concentration or dilution factors due to cooking or processing of food from RAC into food products. These data used in SHEDS-Dietary may come from registrant submission and the peer reviewed literature.

2.3.5 Food Residue Data

SHEDS-Dietary can use point estimates or (empirical) distributions from any source, modeled or measured (e.g., Field Trials, USDA/PDP, FDA/TDS; PRZM-EXAMS). Field Trial Studies are tests conducted by registrants to determine tolerance on Raw Agricultural Commodities. Field trial residues may exceed anticipated residues when the RAC: (i) includes inedible portions (e.g., banana and orange peel, watermelon rind, etc.), (ii) is generally cooked (e.g., pumpkin), and (iii) is established for feed purposes (e.g., field corn vs. cornmeal).

The USDA Pesticide Data Program (PDP; http://www.ams.usda.gov/AMSv1.0/pdp) tests commodities in U.S. food supply for pesticide residues. It has tested over 85 different commodities: fresh/frozen/canned fruit and vegetables, fruit juices, dairy products, grains, corn syrup, nuts, peanut butter, honey, poultry, beef, pork, catfish. PDP has tested for more than 440 different pesticides. Samples are collected by 12 participating States, representing about 50 percent of the Nation's population and all regions.

FDA's Total Dietary Survey (TDS; FDA 1991-2004) (not used for pesticides) is a market basket study program that collects and analyzes ~280 foods for levels of pesticide residues, industrial chemicals, and toxic and nutrient elements. Foods in TDS are prepared as they would be consumed (table-ready) prior to analysis.

2.3.6 Drinking Water Concentration Data

As with the food residue data, SHEDS-Dietary can use point estimates or (empirical) distributions of drinking water concentrations using any source, modeled or measured (Field Trials, PDP, FDA; PRZM-EXAMS, etc.).

Environmental fate models that can be used to predict drinking water concentrations are PRZM-EXAMS and SCIGROW **(**http://www.epa.gov/oppefed1/models/water/**).** The Agency generally uses environmental fate models (e.g., PRZM-EXAMS) to generate predicted drinking water concentrations for pesticides.

2.4 Methods Issues

2.4.1 Issues Regarding Selection of Consumption Database

Since NHANES has not yet focused special attention on children, the CSFII survey continues to have many more food diaries for children. For example, CSFII has 2,972 infant diaries versus 1,971 diaries in NHANES. For children aged 1-2 years old, a population of concern due to potentially high exposures, CSFII has 4,287 diaries vs. 2,460 diaries in NHANES. Another issue is whether or not to use all food diaries, or simply the two day diaries. In contrast to CSFII data, only one day of food intake was collected during the first four years (1999-2002) of the NHANES survey. Therefore, NHANES has a slightly larger total number of one day (only) diaries (N=22,035 subjects) as it does two day diaries (N=16627 subjects, or 33254 person-days).

Some alternative approaches for imputing values for missing data in CSFII have been explored. The two fields of interest are: (i) direct drinking water, and (ii) time of eating occasion. The modeled results appear to be relatively robust with respect to data imputations on these two variables. Approximately 738 diaries, or 1.8% of the total 41,214 CSFII food diaries did not report any information regarding direct drinking water consumption. SHEDS-Dietary (as well as Calendex-FCID and the other models) assume that these diaries did not consume any direct drinking water. DEEM-FCID uses only the 40,476 of the 41,214 CSFII food diaries that responded to this question (may have included people that did not consume any direct drinking water) when conducting drinking water risk assessments; but this subset generally has not affected any of the comparisons with SHEDS-Dietary (drinking water alone, or food+drinking water). For eating occasions, approximately 3,948 records, or 0.6% of the 598,829 food records in the CSFII database had missing values for the time of day question. SHEDS-Dietary replaced those missing values with 12:00 noon since it was the most reported frequency reported, and assumes zero consumption for non-reports in drinking water intake.

2.4.2 Issues Regarding Sampling Food Residues

SHEDS-Dietary allows Monte-Carlo simulations to be based on specific food items, as well as raw agricultural commodities (RAC-FF). Figures 2-1 and 2-2 illustrates this process. If residues are specified for particular food(s) (e.g., cheeseburger), then SHEDS-Dietary randomly draws a residue from that corresponding distribution and ignores any residue data assigned to the ingredient RAC-FF (e.g., beef, tomatoes, wheat, etc.). If residues are not specified for any food item, then the model randomly draws residues for each of the RAC-FF ingredients. The Agency generally requires information at the commodity level, and so this option may be applied to a certain category of food items, such as milk (versus other dairy products), and meats ('steak').

The current version of SHEDS-Dietary randomly draws 1 residue value for each commodity (RAC-FF) and applies that commodity residue to all foods, on all eating occasions. However, the Monte Carlo simulation can draw a new food residue for each eating occasion. The Agency asked the 1999 SAP, "Under what circumstances should the EPA consider using the (DEEM) Eating Occasion approach?" The Panel (1999) noted:

> "Dietary exposure analysis is an extremely complex process. It utilizes many pieces of data from different sources, each carrying its own limitations and deficiencies for the purpose. Therefore, a careful documentation of the database limitations and the uncertainties associated with the estimated exposure is essential for a proper interpretation of the exposure estimates." 1

The qualifying comments reflect a complexity in accounting for differences in eating habits across the population. To illustrate this point, the food consumption diary presented above (Table 2-1) indicates that the 1 yr old consumed the same food ('home fries') on two different eating occasions. It is likely that the child had 'leftovers' in the evening meal. If that is the case (or more home fries were prepared from the same bag of potatoes), then it would be appropriate to assume that the same composite residue was present on both eating occasions. On the other hand, if the child consumed two servings of 'home fries' from different fast food restaurants on two different eating occasions, then it may be more appropriate to randomly draw separate residues for each eating occasion. Such conditional modeling decisions can better made after a closer inspection of the food consumption data. A decision rule based on a few more variables (e.g., food item and primary source of food) may be helpful to determine if different residues should be drawn for subsequent eating occasions, and/or the same residue can be applied to all eating occasions. We have found that this modeling assumption often does not have a significant effect on the 99.9th for food-only exposure assessments – since most people consume various foods on only a single eating occasion as noted in the NMC CRA (USEPA FIFRA SAP 2005, 2007); (Nako, et. al, 2007 ISEA cited earlier).

One of ORD's/OPP's planned activities is to conduct a more thorough systematic review of the food consumption diaries. We anticipate that such analyses may help towards developing decision rules for selecting or not selecting a new residue. For example, if the commodity comes from the same food items, then the model uses the same residue. If not, then the model compares the foods' sources, time of eating occasions, and if the foods were eaten at home. If those factors differ, then the model selects different residues, else retains the same residue. The potential for different decision rules also suggests the development of some type of uncertainty analyses.

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1 FIFRA SAP (2000) Report No. 2000-01B, May 25, 2000, Pages *33-35*.

2.4.3 Modeling Longitudinal Food Consumption

The approach for constructing longitudinal consumption profiles is currently being reevaluated, since the National Health and Nutrition Examination Survey (NHANES) food consumption data does not provide data on calendar dates (season), nor locations (region). Available food consumption data are cross-sectional (2days for an individual). When randomly drawing multiple one-day diaries from multiple individuals that are intended to represent a single individual's behavior over time, the modeler faces a dilemma with optimizing inter- and intra-person variability (see Figure 2-3). If a small number of diaries are drawn for each individual to cover a long simulation period, then each diary must be re-used many times; that is, each diary must be used on many different dates in the simulation to represent the individual's behavior (for dietary exposure, the key variable is total caloric consumption). While this creates repetitive or habitual behavior patterns, it also narrows the behavioral space and lessens the within-person consumptionvariability. Using many different one-day diaries would address these last two concerns by broadening the simulated individual's behavioral space and increasing the within-person variability. However, this approach would exacerbate other problems. In particular, any two persons belonging to the same cohort will draw their diaries from the same diary pools, and the samples will tend to converge to the same overall average behavior of the cohort.

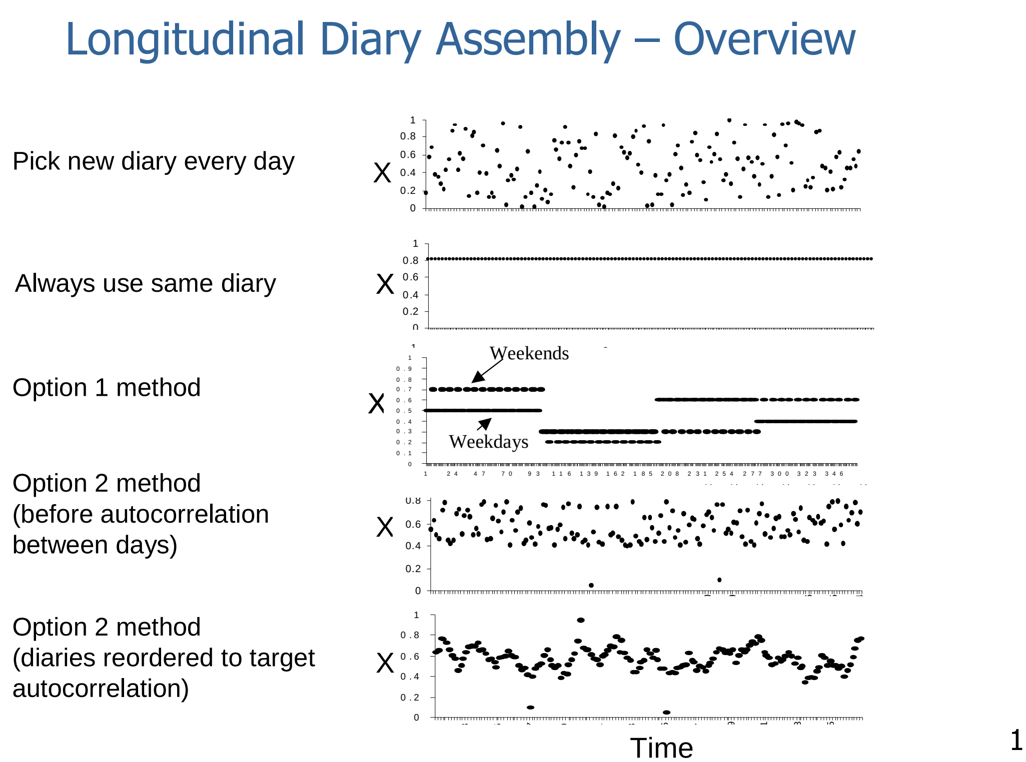

Figure 2-3. Different methods for assembling longitudinal diaries from cross-sectional data

Most of the existing random-draw methods of diary selection assume that all diaries that are suitable (meaning they are from the correct age-gender cohort and match the chosen daytype) are equally likely to be chosen, and that any subsequent draws are independent of prior draws. As detailed in the SHEDS-Multimedia 2007 SAP documents (http://www.epa.gov/scipoly/sap/meetings/2007/081407_mtg.htm, Glen et.al. (2007) proposed a new method for developing longitudinal activity profiles. This "D & A" (Diversity & Autocorrelation) method presented above drops both these assumptions by assigning each simulated person a "target behavior," and then preferentially sampling diaries to produce the target behavior. The method assigns target behaviors and executes the preferential sampling based on the value of D (diversity) specified by the modeler. If not executed carefully, preferential sampling can result in behavioral biases, where some diaries are consistently drawn more often than others. The method contains internal rules for this sampling that ensure that over a large number of simulated persons, all available diaries in each diary pool will be sampled nearly uniformly.

In this method, a new random draw is made for every day in the simulation. Thus, a one-year longitudinal diary would be comprised of potentially 365 different diaries. The D statistic affects the width of the diary selection probability peak around the target behavior, with a low D giving a broad peak and a high D giving a sharp, narrow peak. Depending on the width of this peak and the number of diaries in the pool, some diaries may be selected multiple times, but others may be selected just once or not at all.

The longitudinal data from Lu et al., 2006a,b (Alex Lu, personal communication) were used to develop the D and A statistics needed to apply the Glen et al., 2007 approach for SHEDS-Dietary longitudinal diary construction. We need to model longitudinal food consumption in order to account for chemical half-lives and seasonal patterns in exposures across three primary sources: food, drinking water, and non-dietary exposures from residential uses. The longitudinal dimension does not appear to be critical for obtaining estimates of a single total daily exposure at per capita upper percentiles (see US EPA (2004) for some comparisons). A focus on longitudinal exposures may expand as the Agency continues to develop physiologically-based pharmacokinetic models (PBPK) for pyrethroids and other pesticides. The 2005 SAP noted that one-day simulation models may underestimate risks if carry-over effects from consecutive days of exposures are of concern.2 All three sources (food, drinking water and residential) have a potential for seasonal exposure patterns (positive autocorrelation). We can anticipate strong patterns in drinking water exposures since most people consume water daily, and both the surface water and ground water models generally produce drinking water concentrations that exhibit positive autocorrelation. Similarly, non-dietary exposures from residential uses will reflect seasonal patterns in product usage, as well as correlations in daily activities for a particular

2 FIFRA SAP (2005), Minutes, p.10, "In particular, if one applies a 4.1-fold inter-species scaling factor to the 5.4 hr half-time for reversal of brain AChE inhibition in rats, one obtains a predicted half-time of 22 hr in the 70 kg human adult. Such a long half-time would force the risk assessment model to address carryover of inhibition from one day to the next. In considering this issue, the Agency should take into account cases where there is a dose dependency for inhibition reversal half-lives." p.56.

person. For food, one can conceive an individual purchasing a bag of treated apples, and consuming one or a few apples from that bag over consecutive days.

The relative importance of these three sources (food, drinking water, and residential) vary by chemical, as well as across individuals within a subpopulation. In two companion papers, Lu et. al. (2006a, 2006b) reported that residential uses appear to be more important for exposures to some synthetic pyrethroids, while dietary exposures appear to be relatively more important for some organophosphate pesticides. Their assessment is based on a longitudinal study of 23 elementary school-age children, using urinary metabolites as exposure biomarkers. The researchers collected two spot daily urine samples, first-morning and before-bedtime voids, throughout a consecutive 15-day study period, which consisted of three phases. Children consumed their conventional diets during phase 1 (days 1-3) and phase 3 (days 9-15). During phase 2 (days 4-8), organic food items were substituted for most of children's conventional diet, including fresh fruits and vegetables, juices, processed fruit or vegetables (e.g., salsa), and wheat- or corn-based items (e.g., pasta, cereal, popcorn, or chips) for 5 days. Meats and dairy products were not substituted. A description is provided in the paper: "Parents were asked to request organic foods for their children in phase 2 with the goal of exactly replacing the items the children would have normally eaten as part of their conventional diet. This method ensured that any detectable change in dietary pesticide exposure would be attributable to the organic food rather than a change in the diet."3 The researchers found lower levels of two organophosphate pesticides during phase 2 when organic foods were provided, but no observable change in levels of pyrethroid insecticides. However, they did find a significant correlation between the homeowners self-reported use of pyrethroid products (N=7 household users) and concentration levels of two pyrethroid metabolites (Lu, C. et.al., 2006b).

The literature also contains alternative methods for developing longitudinal consumption profiles; we will consider these in future versions of SHEDS-Dietary. For example, promising effort is described in three papers, authored by a team of researchers from government (NCI), academic and other private institutions. Dodd et.al. (2006) provide a comprehensive review of existing methods used to estimate long-term dietary intake using cross-sectional data. Tooze et.al. (2006) present a new method for estimating long-term intake of episodically consumed foods using food frequency questions (FFQ). A food frequency question (FFQ) is: 'How often have you (respondent) consumed fish during the past 30 days?' Tooze et.al. (2006) present a two stage model, with the first part (logistic regression) predicting the probability of consuming a particular food, and the second part (regression on log transformed consumption amount) predicting the amount of food consumed (>0). In the third paper, Subar et.al. (2006) apply this method to the Eating at America's Table Study (EATS) data. The researchers noted that people that consume foods more frequently (FFQ) also tend to consume greater amounts of that food per occasion. Subar et.al. (2006) also provide a brief review of the development of the Food Propensity Questionnaire, a set of FFQ that was introduced in the 2003-2006 NHANES.

Findings in Givens et al., 2007 suggest a longitudinal dietary survey with minimum 6 consecutive days' dietary consumption in each of 4 seasons would be adequate to represent an

3 Lu et.al., 2006a, p.260.

individual 1 year dietary consumption pattern, and improve cross-sectional approach. "The majority of the Panel is convinced that given the data and analysis presented by the Agency, it is not sufficient to construct the longitudinal dietary consumption pattern based on the 8-day eating occasions." (p. 33 of 2007 SAP). Based on comments by the 8/07 SAP, we prefer using the D&A methodology rather than the 8-diary approach used in the SHEDS-Multimedia residential module.

We will use real data as available to evaluate these different approaches and provide the basis to decide which to use in future versions of SHEDS-Dietary. We anticipate that these and other research activities may help us to improve the current approach for modeling longitudinal consumption, and to develop appropriate uncertainty analyses to characterize the pesticide dietary exposure assessments. In the meantime, SHEDS-Dietary uses the D&A approach for modeling longitudinal food consumption. There are many potential covariates and measures of diversity across many subpopulations. The diet, health and nutrition literature contains a rich volume of research, indicating that food consumption patterns may vary by race, ethnicity, lifestyle (activities and energy requirements) and socio-economic factors.

2.4.4 Considering Persisting Effects

The SHEDS-Dietary Eating Occasion analysis uses the Maximum Persisting Dose (PD) in addition to Total Daily Exposure (for each person-day) to calculate exposure per capita various percentiles e.g. 99.9th. For the hypothetical case below, the Total Daily Exposure is 2 ug/kg (=sum of 2 exposure events), the Max PD is 1.25 μg/kg (Max point on green line) based on a 2.5 hr half-life. The max PD reflects an approximate single bolus dose that produce same level of peak inhibition as the two exposures.

Figure 2-4 depicts a hypothetical scenario in which a person obtains dietary exposures on two eating occasions (e.g., ate 1 slice of watermelon at noon and another at 5 pm). The red triangles depict the amount of exposure (1 μg ai/kg bw) obtained on each eating occasion, while the green line following the first exposure event depicts the Persisting Effect on cholinesterase inhibition. For this example, the recovery half-life is assumed to be 2.5 hours (150 minutes). Therefore, the persisting effect from the first exposure event (1 μg ai/kg bw) is approximately 25% of the peak effect (0.25=(1/2)^(300/150)) when the second exposure event occurs 5 hours (300 minutes) later.

The Persisting Dose reflects the combined effect from the current exposure and the persisting effects from recent exposures. The persisting dose at the second eating occasion amounts to 1.25 μg ai/kg bw (1.25=1+0.25), which is also the Maximum Persisting Dose over this person-day. The Maximum Persisting Dose is interpreted as an equivalent (single) bolus dose that produces the same peak level of inhibition as the exposure patterns from the simulated person-day. This refinement has different effects for different exposure profiles. For the hypothetical scenario above, it reduces TDE from 2 μg /kg bw to 1.25 μg /kg bw. If those exposures occurred on a single eating occasion (e.g., 2 slices at either noon or 5 pm), then this refinement would not affect that particular outcome (Max Persisting Dose=2 μg /kg bw=TDE). This analysis is based on several important assumptions: (i) the time to peak effect is instantaneous (for convenience), (ii) direct drinking water consumption is allocated over 6 fixed events at fixed times, and (iii) the subject (person) is healthy (no carry over effects).

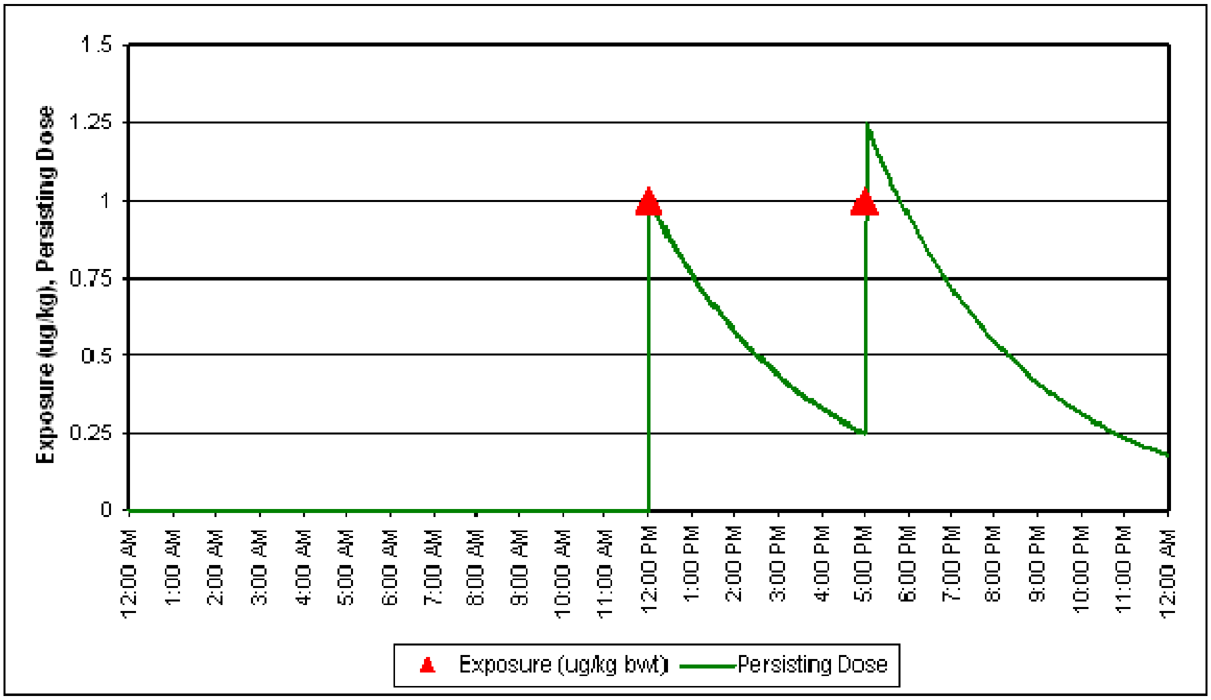

Figure 2-4. Hypothetical Figure to Illustrate Persisting Effect for an Individual

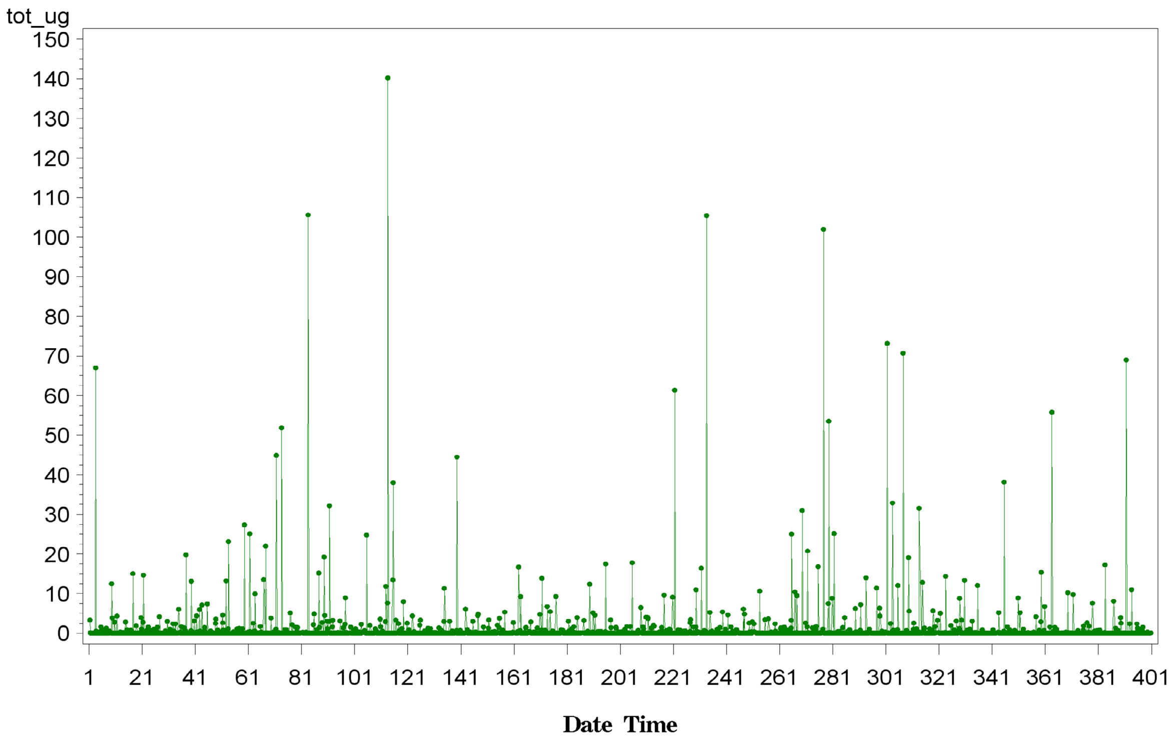

Figure 2-5. Example SHEDS-Dietary modeled longitudinal dietary exposure profile for 1 individual

Figure 2-5 shows an example longitudinal dietary exposure profile for one individual using SHEDS-Dietary. The persisting dose (green line) was modeled from a cumulative data analysis using the chemical half lives.

2.4.5 Algorithm for Matching (Behavioral) Diaries: Food Consumption and Activity Patterns

It is a challenge to merge dietary and residential exposures because the behavioral data are from different sources. It is more complicated for the longitudinal data. Bins by important variables are used to merge the data; a balance between number of key variables and randomization has to be controlled. Too many variables used to form bins will reduce the randomization and too few variables will increase randomization but increase misclassification between the dietary and residential exposures. An average of 50 to 100 data points in each bin is used as a criterion to select the key variables to make sure that we have enough sample size in each bin for the randomization. Key variables are age, gender, body weight, total caloric intake/METS, race, season, weekday and region. The D & A method described above (see bottom of figure 2-3) uses total calories to turn the cross-sectional dietary exposure into longitudinal food consumption patterns, and uses waking time at home to turn the residential cross-sectional activity patterns into longitudinal patterns. Then age, gender, body weight, total caloric intake/METS, race, season, weekday and region can be used to form the bin to match dietary and residential exposures. A proposed methodology for matching food consumption and activity diaries, to merge SHEDS-Multimedia dietary and residential modules, will be presented to the EPA FIFRA SAP in July, 2010. This methodology, described later in this manual in the section entitled, "Algorithm for Matching (Behavioral) Diaries: Food Consumption and Activity Patterns." has been tested through "soft linking" the two modules with a permethrin pesticide case study.

2.4.6 Considering Timing and Amounts of Drinking Water Consumption

SHEDS-Dietary utilizes the CSFII or NHANES data to assess the timing and amounts of **indirect** drinking water intake (i.e., through foods, infant formula, 'kool aid', coffee, tea, etc.) within a simulated person-day. The model contains two options for allocating **direct** drinking water consumption (i.e., through tap or bottled water) throughout the day: (1) fixed approach, and (2) empirical using the recent NHANES data or the Bayer DWCS data described above. In the fixed approach, SHEDS allocates the CSFII respondents' total direct drinking water consumption (mL/day) over 6 fixed occasions (6:00 am, 9:00 am, 12:00 noon, 3:00 pm, 6:00 pm, and 9:00 pm. Preliminary analyses revealed that there is no significant difference between these two approaches.

The second option uses the Bayer DWCS data to allocate the total amount of **direct** drinking water consumed throughout the simulated person-day.[4] This procedure involves the following steps:[5]

1. Generate cohort ('bins') by gender, age, season
2. For each DWCS diary, calculate the percent of Total Direct DW, by Occasion
3. For each CSFII or NHANES diary, randomly select a Bayer DW diary from appropriate 'bin'
4. Use Total Direct DW from CSFII or NHANES and percentage of DW from DWCS data to calculate direct DW amount for each Eating Occasion (time of occasions also from DWCS)

This second option cannot be applied for the infant subpopulation since the DWCS data did not include infants. Although the DWCS study did not appear to have the same level of sophistication as the CSFII in its sampling design, our expert view is that these data are useful to model the timing of direct drinking water intake for several reasons, including: (1) the marketing firm, the NPD group, has extensive experience at monitoring eating and drinking trends in the US and Canada, (2) the design of the data collection instrument, i.e. recording consumed amount of water for each drinking event, led to better 24 hour recall, (3) reasonable response rates

4 The Panel noted: "In further development of this approach, EPA should make use of any reliable source of relevant empirical data on daily patterns of drinking water consumption; ideally adapted to the likely consumption behavior in specific regions or smaller areas of the country." P.59 of 63, SAP 2005b.

5 This algorithm can be modified for longitudinal models, 'binning' respondents (persons), rather than diaries (person-days) to retain the intrapersonal information contained in these 7-day drinking water diaries.

(>30%), and the relatively high percent of respondents that completed 7 day diaries (82%), and (4) the 7 day study period reduces the need to model intrapersonal variability over this duration.

An alternative method being considered for using the drinking water data is a two step approach for each simulated person: (1) randomly draw one of the 30 years, and (2) apply the predicted concentration for January 1st of that selected year to calculate exposure for Day 1, and so on, with predicted concentration on December 31st being applied to calculate exposure for Day 365. This general approach, available in other aggregate models, has the advantage of retaining autocorrelation present in the predicted drinking water concentration data.

Figures 2-6 and 2-7, taken from DWCS report (Figures 5 and 6, respectively), indicate that many respondents consume direct drinking water on multiple occasions, and at all times throughout the day. This provides some support for using a simple modeling assumption (e.g., equal amounts allocated across 5 or 6 occasions). Those distributions do not reflect variations in drinking water intake across individuals. The report suggests that these data may be used to model drinking water exposures, by eating occasion:

> *"It may be possible, using the information collected by the DWCS to "allocate" the total daily water consumption amount reported in the CSFII into various drinking occasions. Specifically, if each subject in the CSFII survey was randomly matched to subjects in the DWCS, based on survey season, region, age, gender, and total amount of drinking water consumed per day, then the total amount reported by that CSFII participant can be allocated to the same number of drinking occasions as those reported by the matching DWCS participant. Similarly, the proportion of the total daily water consumption allocated to each of these drinking occasions can be assumed to be similar to that reported by the matching DWCS participant. This approach would then allow a less than 24-hour assessment of both food and drinking water (aggregate assessment) for a pesticide."* [6]

[6] Barraj, L.M. et.al. (2004), Exponent®, Inc.; National Product Database (NPD) Group., p.17.

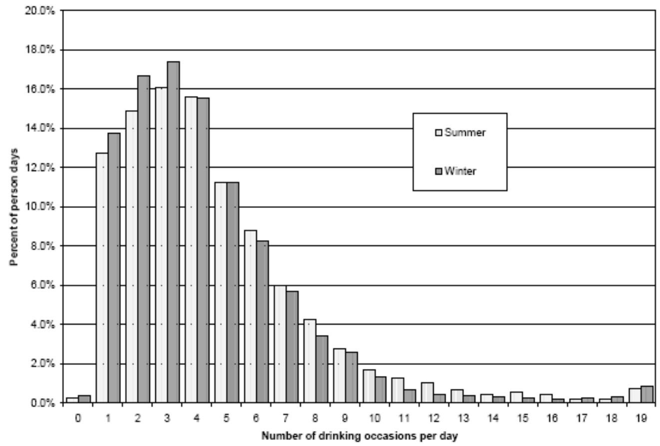

Figure 2-6. Total Number of Occasions of Direct Drinking Water Consumption

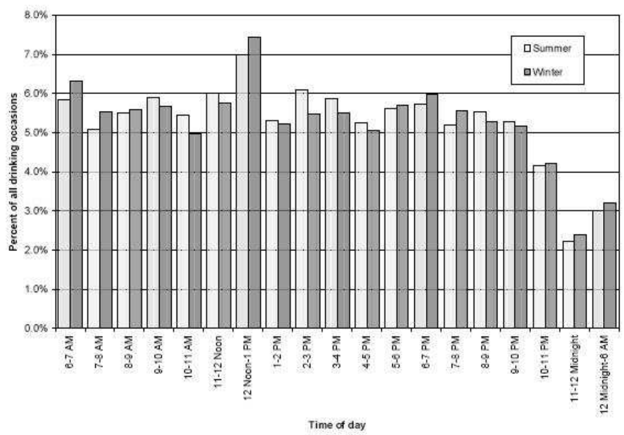

Figure 2-7. Distribution of Direct Drinking Water Consumption, By Time of Day

Table 2-5 provides the total number of drinking water diaries in the DWCS by gender, age and season. Infants less than one year old were not included in this survey. The two adult bins (20-49 yrs, 50+ yrs) contain a large number of diaries since they encompass a greater range of years. The DWCS contains a relatively large number of drinking water diaries for most of the children's 'bins'; the one-year old female, summer bin has the fewest number of diaries (N=29).

Table 2-5. Total Number of DWCS Diaries, By Age Group, Gender and Season

Age Group	Gender	Season		Subtotal	Subtotal
		Winter	Summer	Age-Season	Age Group
1 yr	M	98	128	226	391
	F	136	29	165	
2 yrs	M	167	97	264	462
	F	125	73	198	
3 yrs	M	132	81	213	453
	F	151	89	240	
4 yrs	M	128	63	191	438
	F	149	98	247	
5 yrs	M	141	109	250	380
	F	67	63	130	
6-12 yrs	M	663	404	1,067	2,148
	F	624	457	1,081	
13-19 yrs	M	491	322	813	1,758
	F	577	368	945	
20-49 yrs	M	2,871	1,999	4,870	11,450
	F	4,036	2,544	6,580	
50+ yrs	M	1,975	1,688	3,663	9,712
	F	3,332	2,717	6,049	
Total	M	6,666	4,891	11,557	27,192
	F	9,197	6,438	15,635	

The DWCS raw data files did not include sampling weights to make projections at the per capita level. The report noted that the estimated direct drinking water intakes reported by the DWCS respondents were slightly higher than the 1994-1998 CSFII respondents. For example, the overall mean intake of DWCS respondents was 37.8 oz/day (40.6 oz/day =summer, 35.7 oz/day =winter)[7], while the CSFII respondents reported 29.6 oz/day (32.4 oz/day =summer, 27.8 oz/day =winter).[8,9] While no formal statistical tests were presented, the report noted that this difference may be due to the fact that "the DWCS provided participants with a time grid to report their water consumption, thus potentially helping them remember all their water consumption occasions, in contrast to the CSFII general 24 hour total consumption recall question."[10]

In future versions, we plan to utilize the reported time of water consumption data from recent NHANES.

[7] 1117.9 ml/day, 1200.7 ml/day, 1055.8 ml/day respectively
[8] 785.4 ml/day, 958.2 ml/day, 822.1 ml/day respectively
[9] Barraj, L.M. et.al. (2004), Table 7, p. 26. Figure 5 provides some estimates, by age groups. (p.31)
[10] Barraj, L.M. et.al. (2004), p.16.

2.4.7 Considering Number of Person-Days (or Person-Years) to Simulate

Agency risk assessors typically specify 1,000 iterations per diary during a DEEM-FCID simulation, providing for about 41 million person-day simulations (=41,214 person-day diaries x 1000 iterations/diary). Except for extremely unusual circumstances, this number of iterations has provided very stable results at the per capita 99.9th percentile for all subpopulations (i.e., not much 'simulation' or 'random seed' uncertainty). Similarly, users can specify any number of iterations per diary using SHEDS-Dietary (cross-sectional). The sensitivity analyses presented in this section were based on only 150 iterations which appeared to be sufficient to verify results with DEEM-FCID. We specified fewer iterations since SHEDS-Dietary (for cross-sectional analyses) retains all of the output from each simulated person-day (creating 4 GB in output with 150 iterations), allowing sensitivity analyses to be conducted much more efficiently. ORD/NERL has not developed recommended number of person-years for SHEDS-Dietary.

2.4.8 Sensitivity Analysis Issues

The most difficult part of conducting sensitivity analyses is in the problem formulation: defining a particular issue of concern, evaluating the available data inputs, developing method(s) to assess how sensitive the results are to that concern, and characterizing the degree to which that analysis addresses that concern. More details are provided below in the section, "Sensitivity Analyses Methods."

2.4.9 Uncertainty Analysis Issues

Uncertainty analyses may help ascertain the relative importance of the data inputs. There is uncertainty in estimates of a total single-day exposure from various factors, including: limited food consumption data (CSFII), food recipes (FCID), available residue data (e.g., PDP monitoring, crop translations), and processing factors. This preliminary list of factors expands with longitudinal measures and the use of PBPK models. To date, OPP has not utilized formal uncertainty analyses in its pesticide dietary exposure assessments.

2.5 Output Capabilities

SHEDS-Dietary can be used to estimate population distributions (and select percentiles of interest such as 95th, 99th, 99.9th) of aggregate or cumulative dietary exposures, and generate the following output results:

- CDFs of dietary exposures for populations of interests, including food and water separate or combined, as well as by eating occasion;
- Bar charts, pie charts, and summary tables showing contribution to total exposure (e.g., 99.9-100th), by food, commodity, or commodity-chemical (for multi-chemicals);
- Summary statistics of dietary (food, drinking water, or sum) exposure by age group and/or gender (including females 13-49 yrs old); and
- Eating occasion, sensitivity, and uncertainty analyses to identify key factors.

A summary of various SHEDS-Dietary outputs and analyses is given in Table 2-6.

Table 2-6. Potential Applications of the SHEDS-Dietary model

Variable/Modeling	Description
User-only Analysis	
Eaters-only Report	Deterministic calculation of exposures among people that consume a treated commodity or food
Contribution Analysis	
Shares of Total Exposure, by Commodity, Food or Diaries	Current reports provide shares of total exposures (99.9th – 100th percentiles), by commodity or by food
Shares of Total Exposure, by Chemical – Commodity, Food or Diaries	For cumulative exposure assessments, SHEDS keeps track of residues, by chemical (i.e., not used RPF combined residue)
Shares of Total Person-days, by Commodity, Food or Diaries	(i) 'Exceeders' or shares of total person-days (99.9th – 100th percentiles), by commodity. (ii) focus on diaries: percent of simulations exceeding target
Sensitivity Analysis	
Consumption 'Outliers'	Effect of Diaries with Reported High Amounts Consumed
Percent Samples Treated	Effect of the Estimated Percent of Samples Treated (Half Level Of Detection (Half-LOD) used for monitoring data)
Percent Crop Treated	Effect of Annual Fluctuations in Percent Crop Treated (assuming all other factors constant)
Processing Factors	Effect of Estimated Processing Factors
Uncertainty Analysis	
Uncertainty - Cohorts	Effect of Different Factors for Developing 'Cohorts' or 'Bins' for Food Diaries
Uncertainty – Subsamples	Effect of using a Subsample of the Food diaries and Residue data on per capita estimates (200 person-years)
Uncertainty – Subsamples of residues, by commodity	Residue by commodity
Uncertainty – Models	Comparing Results Across All Models

The SHEDS-Dietary module retains detailed person-level outputs for each dietary exposure assessment. Presently, the SHEDS-Dietary Cross-Sectional simulations retain more detailed information than the SHEDS-Dietary Longitudinal simulations. For the Cross-Sectional simulation, the SHEDS-Dietary module retains detailed information for each exposure event, including food diary ID, time of eating occasion, food item, FCID commodity (RAC-FF), amount consumed (g), residue (ppm), and exposure (ug ai). Since the CSFII and NHANES\WWEIA surveys contain numerous food diaries, a Cross-Sectional simulation specifying 200 iterations for each of the 40,214 CSFII diaries will generate 8,042,800 person-day outcomes (=40214x200), which may take up to 10 GB of hard disk space. To facilitate data processing, SHEDS-Dietary splits the outputs into multiple data tables. In the example above, the outputs from a SHEDS-Dietary cross-sectional simulation would be stored 200 separate tables in the SAS library 'Output', and the filenames for each table will start with the prefix as provided by the User.

The outputs from a SHEDS-Dietary longitudinal simulation are currently stored in a single table in the SAS library 'OLONG', with the filename starting with the prefix as provided by the User followed by the suffix (long) (e.g., SAS data table for case Study #3: Olong.Cperm_long). The results retained in the longitudinal simulation include: person ID, date, food diary ID, total calorie, time of eating occasion and exposure (ug ai). The data fields and formats for the cross-sectional and longitudinal simulations are provided in the SHEDS-Dietary User Guide, Appendix 3.1 (cross-sectional simulations), and Appendix 3.2 (longitudinal simulations). Since commodity level details are not retained in the longitudinal simulation, the contribution analyses is limited compared to 'cross-sectional' simulations. {We will consider outputting detailed results in future versions; perhaps saving the results for each modeled person in a separate table (file) to ensure that the data tables are not too large for data processing.}

There are several advantages and disadvantages of retaining all of the detailed data. The primary disadvantage is that a single simulation may take up a considerable amount of hard disk space (8+ GB); if users need to perform simulations for multiple chemicals, then this may pose a significant issue (e.g., the hard disk on the Agency's laptops have 80 GB capacity). Another disadvantage is that appending data to the output tables may increase the processing time considerably as those tables become increasingly larger. If the user is only interested in knowing aggregate daily exposure at some per capita percentile (e.g., 99.9th), then processing time can be shortened since the model only needs to retain total daily exposure for each simulated day.

The advantages for retaining the detailed outputs for each simulated person-day, include: (i) querying/viewing detailed outputs for select diaries and/or persons, (ii) perform alternative methods for assessing contributions (exceeders), (iii) facilitate sensitivity analyses ('what-if' scenarios), (iv) conduct sensitivity analyses (outliers), (v) perform 'eating occasions' analyses for multi-chemical assessments, (vi) pass on dietary exposures by time of day to PBPK model.

We describe two of these advantages below. First, it is important to recognize that the user can query these output tables to calculate aggregate dietary exposures at various per capita percentiles, as provided in the "Exposure and %APAD: Summary Table". Suppose the user wants to know how aggregate exposure at the per capita 99.9th percentile changes if we removed that pesticide's use on lettuce. Then, the user could either zero out residues for lettuce and rerun the simulation, or zero out the exposures from the simulation and recalculate the 99.9th percentile. The first option will take considerable processing time (especially in a cumulative setting) and add simulation uncertainty since a new set of residues is randomly selected for each person-day-food. The latter option is more efficient since the model simply recalculates the 99.9th percentile with the existing results - zeroing out exposures from that particular commodity. The user can submit a batch job to perform such 'what-if' scenarios for various combinations of foods (e.g., removing only lettuce, or removing only apples, or removing apples+lettuce, etc.).

The second example, described in further below, is performing sensitivity analyses to assess potential uncertainties (measurement error) regarding reported food consumption. Nako and Xue (2006) identified several food consumption diaries that reported high drinking water intake, and wanted to assess the effects of those diaries upon the per capita 99.9th percentile. The user needs to first identify which food consumption diaries are of concern and what adjustments are to be made (e.g., drop diary altogether or adjust the reported consumption). Once that determination is made, the simulated exposures can be adjusted accordingly, and the per capita 99.9th percentile recalculated from the adjusted outcomes. Since SHEDS-Dietary retains the outcomes, the user can perform such sensitivity analyses without 'changing' the underlying food consumption data base. The user needs to use supplemental SAS code (Macros) to conduct such analyses since the Agency had difficulty incorporating these options into the SHEDS-Dietary version 1.0 GUI.

2.6 Sensitivity Analysis Methods and Results

2.6.1 Sensitivity Analyses Methods

The following sensitivity analyses have been run using SHEDS-Dietary v1:

- key data to determine their impact, such as using CSFII vs. NHANES/WWEIA consumption data or PDP vs. TDS residue data;
- different algorithms to assess the impact such as allocating drinking water consumption equally over 6 fixed eating occasions vs. using information from the Bayer Drinking Water Study (discussed below);
- different residue sampling algorithms such as filling in non-detects with zero, half detection limit, detection limit);
- outliers – impact of keeping or removing "outliers" on the key exposure output parameters (e.g., exposure); and
- mitigation -- assessing impact of removing one or a group of RACs (e.g. delete one commodity such as a particular fruit to see the impact on the average and high exposure percentile).

The sections below show results of sensitivity analyses on food and drinking water consumption outliers. Other analyses are illustrated in the case studies of Chapter 3.

2.6.2 Sensitivity Analyses on Food Consumption 'Outliers'

A component of the Agency's risk characterization is to "Evaluate the tails of the food exposure distribution to verify that unusual consumption patterns are not inappropriately impacting on the results of the assessment."[11] Identifying 'unusual' consumption patterns requires inspection of the food diaries. If the amounts consumed are not unreasonably high, then no further analyses is required. As the panel noted,

> "*The CSFII is designed to be representative of the population as a whole. Hence the "tails" of the distribution are still part of the distribution and, therefore, cannot be said to impact the results of the assessment inappropriately.*"[12]

If consumption values are so unusual so as to bring into question the accuracy of the data (e.g., measurement or data entry error), then quantitative 'what-if' analyses may be appropriate. A question for the exposure modeler is how sensitive are exposures at the upper per capita

[11] EPA SAP, 2005, p.187.
[12] SAP minutes, 2005, p.36.

percentiles to one or a few such data records? The open source coding of SHEDS-Dietary enables the user to perform such analysis in a quick and cost-effective manner.

Figure 2-8 presents a Box and Whisker plot of potato consumption among children ages 1 and 2 years old. The amount of potatoes consumed by the CSFII diary highlighted earlier (Table 2-1; ID=28517-2-2) is about twice as high as the second highest eater in this age group. This amount appears to be an outlier when focusing on only 'fried' potato consumption, but not so much the case when considering potato consumption in other food forms (e.g., boiled). As absolute amount consumed, this amount does not appear to be implausible: a 1 yr old, 13 kg boy eating 300 grams of home fries on two occasions. But a considerable amount of resources may be expended to defend that assessment, and using the SHEDS-Dietary model, we can determine that the per capita estimates are fairly robust to this one diary. In particular, if we either (i) removed this 'outlier' from the Monte-Carlo simulations, or (ii) adjusted the amount consumed to lower level (e.g., second highest amount), the per capita estimates at the 99.9th percentile will not change considerably.

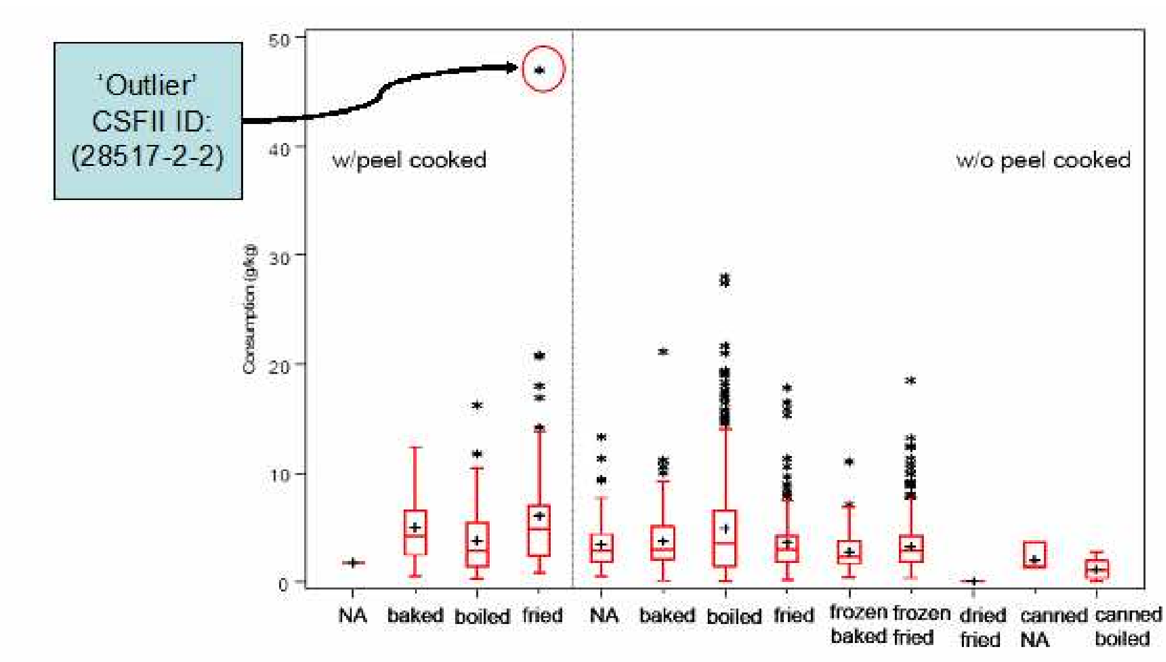

Figure 2-8. Box-and-Whisker Plot of Potato Consumption by Day for Children 1-2 Yrs. Old

2.6.3 Drinking Water Consumption Outliers

As in the case of various food items, there are some high reported drinking water consumption amounts in the CSFII. Figure 2-9 presents a Box-Cox transformation of drinking water consumption (ml/kg bw/day) for all infants in the CSFII data base. The two highest amounts are located in the upper right hand corner – deviating above the otherwise linear pattern established by the majority of the remaining reported consumptions. These two values are, respectively, 52% and 41% higher on a ml/kg bw basis than the next (third) highest reported consumption value. An inspection of the food diaries indicate that a set amount of formula was reportedly prepared and consumed by these two infants on multiple occasions throughout the day. The first infant diary (28892-2-1) was for a newborn (0 month old) weighing 3.2 kg, that reportedly consumed a total of 1,997 ml that day (1819 mL indirect, 117 direct), or about 624 ml/kg bw/day.

An inspection of the CSFII diary indicated that this infant consumed a total of 8 oz of formula (6 ounces consumed directly + 2 oz used to prepare 0.25 cup of dry rice cereal) at 8:00 am, 9:30, 11, 1:30, 4:30, 6:00, 10 and 11:30 pm; an additional 4 oz of formula alone was prepared/consumed at 1:00 am. The second infant-dairy (26837-3-2) was a one month old that weighed 3.6 kg, and consuming a total of 2,044 ml that day (1,926 ml indirect, 118 direct), or about 568 ml/kg bw/day. An inspection of this second diary indicate that that infant consumed 8 oz of formula on nine different occasions throughout the day, at 4:00 am, 6:00 am, 8:00 am, 10:00 am, 12:00 pm, 2:00 pm, 6:00 pm, 8:00 pm and 10:00 pm. These two drinking water intake amounts appear to be ‘outliers’ based on the available references, and a brief review of the pediatric literature (e.g., U.S. EPA, 2008).

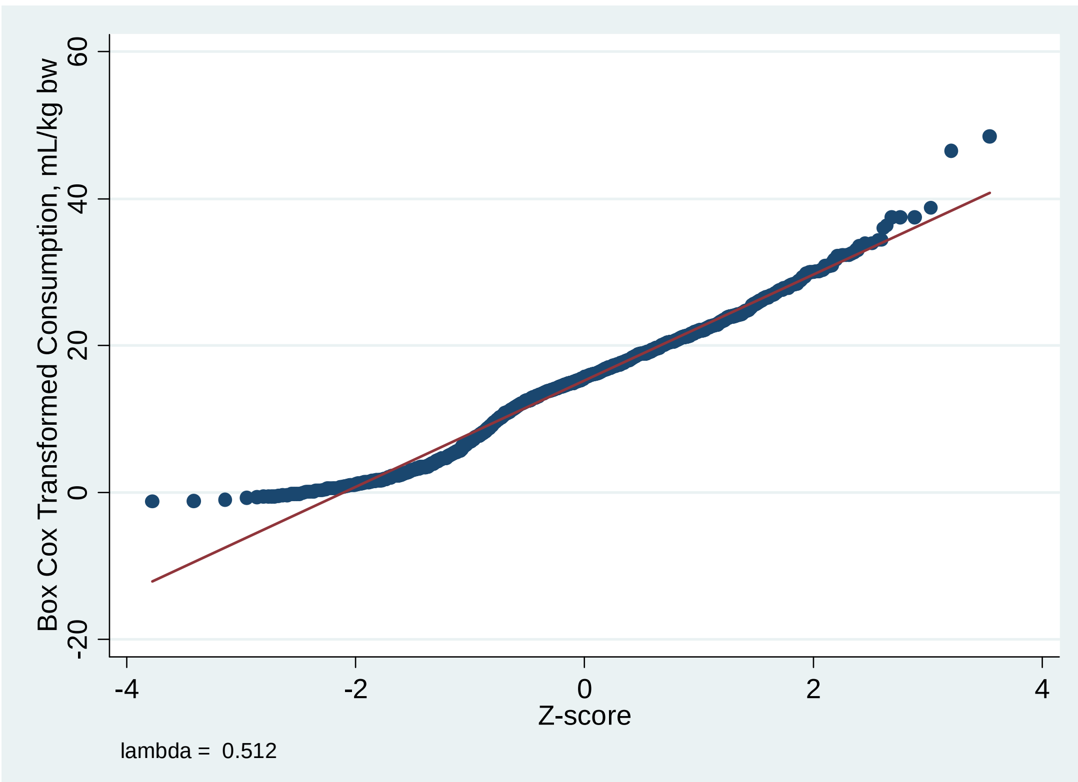

Figure 2-9. Box-Cox Plot of Infant Direct Water Consumption (mL/kg bw/day)

Analyses of the SHEDS-Dietary simulated output for the infant subpopulation indicated that two food diaries constituted about 70% of all high simulated outputs in the top 0.1% of simulated person-days. Again, the question of concern was how sensitive are the estimates at the upper percentiles to the drinking water intakes reported for these two respondents. Agency staff used (cross-sectional) SHEDS-dietary to conduct two 'what-if' scenarios: (1) drop these two diaries from the Monte Carlo simulation, and (2) reduce the reported amounts consumed by 50 percent. Neither of these resulted in marked changes in the estimated exposures at the per capita 99.9th percentile. The sensitivity analyses for the potato eater and these high infant water intake diaries,showed similar insensitivities to these 'outliers.' The Agency previously noted the robustness of the results to residue outliers:

"*…it is often not the extreme upper tail of a residue distribution which is responsible for driving the 99.9th or 99th percentile exposure levels, but rather a combination of reasonable (but high end) consumption and reasonable (but high end) residue levels of one or two frequently consumed agricultural commodities.*" US EPA (1999), pp. 21-22.

While that quote referred to **residue** 'outliers', the two case studies above suggests that a similar level of robustness appears to hold for consumption 'outliers' as well. While such analyses cannot be performed if the consumption diaries are fixed in the code, the open source code of SHEDS-dietary provides agency modelers with complete access to all of the underlying data and algorithms. This feature enables the Agency to quantitatively address other questions that risk managers may have as PBPK models are used to assess dietary risks to pesticides and other chemicals.

Examples of other sensitivity analyses are presented in Chapter 3.

2.7 Uncertainty Analysis Methods and Results

2.7.1 Uncertainty Analysis Methods

SHEDS-Dietary has a simple bootstrapping method for conducting uncertainty analyses - utilizing only a subset of the consumption and residue data inputs. This proposed method is designed to gain some insight about 'How much better would our estimates be if we had **more** data?', by conducting the uncertainty analyses in the other direction 'How far off will our estimates go if we used only a subset of the consumption and/or residue data?'.

The SHEDS-Dietary bootstrap procedure to conduct uncertainty analysis entails the following:
1) Randomly draw certain percentage (e.g., 50%) of person-day from CSFII data or/and randomly draw certain percentage (e.g., 50%) of residue data from pollutant residue files by raw commodity and food form. Run 100 times for variability.
2) Repeat step 1 many times, e.g., 200 times.
3) Quantify variability from each run.
4) Conduct uncertainty analyses from different runs (e.g. 200 times). 200 50th, 95th and 99th values can be acquired respectively. The ratio of 95th vs. 5th percentile of a given percentile can be used to evaluate the uncertainty. The bigger the uncertainty ratio, the bigger uncertainty produced by subsets of dietary and residue data.
5) Obtain important sources contributing to the total uncertainty (e.g., structure, scenario).

To check whether there are enough data for consumption and residue data sources, and which data set was relatively more important for exposure, uncertainty analyses applying statistical bootstrapping of certain percentages of both data sets, were conducted with SHEDS-Dietary for permethrin, as shown in the table and figure below.

2.7.2 Uncertainty Analyses on Selection of Food Consumption Diaries

This section describes SHEDS-Dietary uncertainty analyses focusing on the selection of food consumption diaries. It includes uncertainty analyses for the permethrin application (assessing impact of residues vs. consumption, and sample sizes; assessing impact of number of exposure days before dose results stable).

Figure 2-10 shows the uncertainty for 3 CDFs for bootstrap sampling of 50% of residues and 20%, 50%, 80% of food consumption data. The CDF of the 50% of residues and 20% of consumption data has the biggest uncertainty. It presents uncertainty results for daily dietary cis-permethrin exposure, based on bootstrapping 200 times. The ratio of 97.5th percentile to the 2.5th percentile (95% confidence interval) is 15.07/4.63=3.3. In the same way, we can calculate those ratios for other schemes of bootstraps to evaluate what are the major factors contributing the overall uncertainty.

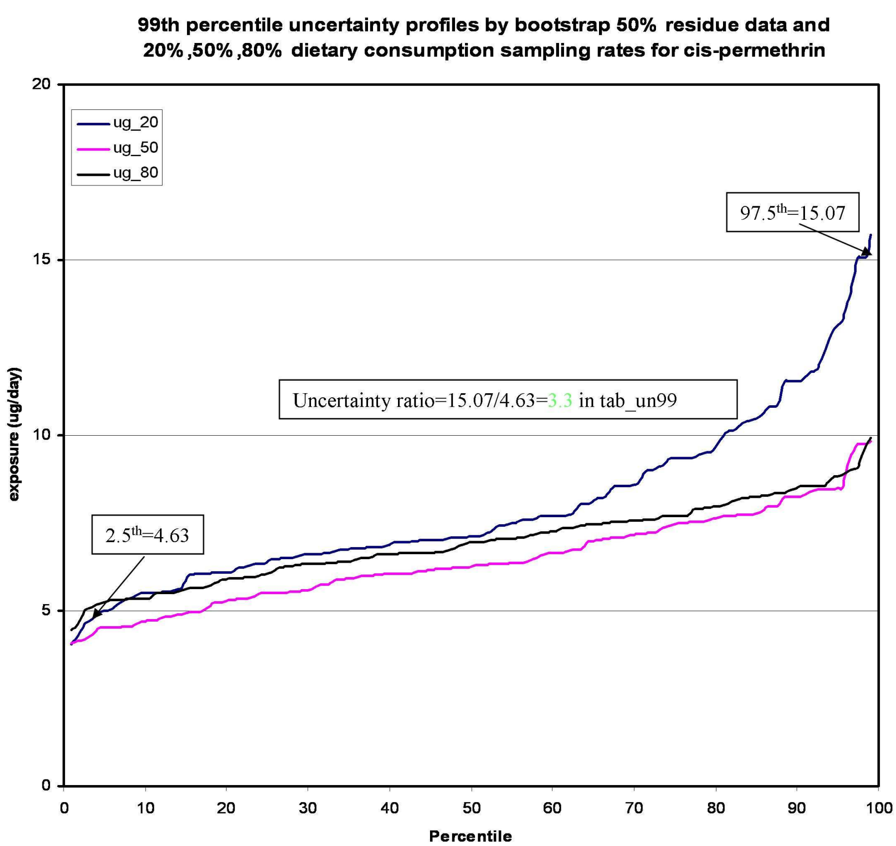

Figure 2-10. Uncertainty analysis profiles for daily dietary cis-permethrin exposure.

Table 2-7 shows results of uncertainty analyses. The green highlighted cell (3.3) reflects the $95^{th}/5^{th}$ percentile ratio for an uncertainty run that used subsets: 50% cis-permethrin residue by RAC, and 20% of NHANES dietary consumption data for 3-5 year-olds. The NHANES food consumption data base contains a total of 6,204 food diaries, and only a subset of those diaries are selected for each simulation (6204*0.2=1241). We ran this 100 times, for a sample size of 124,100 for variability for the same subset. We then ran another 100 times for uncertainty for the different subsets with the same bootstrap sampling rate, yielding sample size of 12,410,000. The 99^{th} percentile was calculated from that simulation, and the process was repeated 100 times, producing one hundred estimates of aggregate exposure at the per capita 99th percentiles. From these 100 values we found the 97.5^{th} and 2.5^{th} percentiles; their ratios yield the uncertainty ratio, 3.3 (15.07/4.63, see Figure 2-10). The bigger the uncertainty ratio, the bigger uncertainty produced by subsets of dietary and residue data.

Table 2-7. Bootstrap uncertainty analyses for cis-permethrin

Ratio of 97.5th v.s. 2.5th percentile of uncertainty 99th CDFs by various percentage of bootstrap

dietary sampling	Bootstrap sampling percentage for cis-permethrin residue data								
percent	10	20	30	40	50	60	70	80	90
10	5.3	3.2	3.6	3.4	4.7	3.5	4.3	4.6	3.3
20	2.8	2.5	3.4	2.5	3.3	3.1	3.5	2.5	2.6
30	2.5	2.3	2.3	2.8	2.5	2.5	2.7	2.3	2.6
40	1.9	2.1	2.2	2.1	2.1	2.0	2.0	2.2	2.0
50	2.3	2.4	1.7	2.2	2.3	2.3	2.0	1.9	1.9
60	2.0	2.1	2.0	1.8	1.9	1.8	1.6	2.2	2.2
70	1.8	1.9	1.8	2.1	1.9	2.2	1.9	2.0	2.0
80	2.1	1.9	1.8	1.8	1.8	1.7	1.8	1.7	1.9
90	1.7	2.0	1.8	1.8	1.7	2.0	2.0	1.9	1.8

2.8 Quality Assurance

Three types of quality assurance have been conducted with SHEDS-Dietary. First, ORD and contractor Alion followed the SHEDS QAPP (US EPA, 2010) when developing the code and GUI. Second, ORD evaluated the model for Arsenic (Xue et al., 2010). Third, OPP provided an independent review, and conducted a comparison of results to the DEEM-FCID model (model-to-model evaluation), as described below.

2.8.1 Comparison SHEDS vs. DEEM (Model-to-Model Evaluation)

This section compares SHEDS-Dietary and DEEM-FCID. Table 2-8 presents the per capita estimates for chemical 'ABC' at upper percentiles (95^{th}, 99^{th}, 99.9^{th}) used by the Agency in acute dietary risk assessments. Figure 2-11 presents the per capita estimates for chemical 'ABC' at the 99.9^{th} percentile for nine subpopulations for 17 separate drinking water scenarios. The differences should reflect only simulation uncertainty (i.e., differences due to different draws of random numbers) since the models both rely upon the CSFII sampling design.

The Panel previously noted the importance of respecting differences due to model uncertainty.13 SHEDS-Dietary was developed to evaluate the incremental effects of specific modeling assumptions. This tool can also help explore other issues, such as the sensitivity analyses as discussed above, as well as other types of analyses that may be requested as the Agency progresses toward using PBPK models.

We briefly describe the DEEM-FCID model since the Agency has generally relied upon this model to conduct dietary risk assessments under FQPA. For each food diary, DEEM-FCID applies a Monte-Carlo simulation to calculate total daily exposure, as depicted by Equation (1).14 DEEM-FCID conducts a fixed number of 'iterations' to each food diary, allowing the user to specify the number of iterations per diary. Agency risk assessors typically run DEEM-FCID with 1,000 iterations per diary.15 DEEM-FCID keeps track of the total daily exposure for each simulated person-day, and applies the corresponding CSFII survey weights to project the simulated person-days to a per capita level. If the user specifies only one iteration, then the per capita percentiles would reflect interpersonal variability – variation in exposures across the subpopulation due to differences in food consumption. If multiple iterations are specified, DEEM-FCID treats each modeled person-day as separate (independent) simulation. The per capita estimates reflect both intrapersonal variability and interpersonal variability. Note that the purpose of these Monte-Carlo simulations is to obtain an estimate of a high-end aggregate total daily exposure.

Table 2-8 presents DEEM-FCID and SHEDS-Dietary estimates (cross-sectional) of total daily exposure at selected percentiles for chemical ABC, for 9 subpopulation groups. Table 2-8 suggests that these two models produce similar results across these subpopulations for this particular set of anticipated (food) residues. Children often have higher exposures than adults

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13 US EPA – FIFRA SAP Minutes 2004-04, p. 24.
http://www.epa.gov/oscpmont/sap/meetings/2004/index.htm#april.

14 The Monte Carlo procedure draws a residue for each RAC-FF. While a particular commodity (Potato, tuber w/peel) may be used in multiple foods, the cooking method may differ, and thus, it will have a different food form. The food form for potatoes used in 'White potato, home fries w/Lard' is 'cooked-fresh-fried' (ff=213, see legend in Table 1). This particular diary may have contained other foods with 'Potato, tuber w/peel' - some of which may have the same food forms, e.g., 71411000- 100701='White potato skins, with adhering flesh, fried, with cheese and bacon', while others have different food forms, e.g., 71603010='Potato salad', 71101110='Baked potato'. If the cooking method is the same (e.g., ''Pork fat' or 'Lard' used to fry eggs and home fries), then the same residue is applied to all those consumption amounts ('home fries', 'White potato skins', etc.). But if the food forms are different (e.g., 'Potato salad' is boiled, ff=212; 'Baked potato', ff=211), then a different residue is independently drawn and applied for those food forms in the total daily simulation.

15 Risk assessors may increase this to 5,000 or more iterations if the results are sensitive at this level.

(mg ai/kg bw/day) at these upper per capita percentiles due to higher intakes of many foods as a percent of their bodyweight.

Table 2-8. A Comparison of DEEM-FCID and SHEDS-Dietary Exposure Results for Chemical ABC.

DEEM-FCID results (1 simulation w/1000 iterations)			
	95th Pctile	99th Pctile	99.9 Pctile
Subpopulation	**(mg/kg/day)**	**(mg/kg/day)**	**(mg/kg/day)**
U.S. General	0.00209	0.01076	0.04873
All Infants (< 1 yr)	0.00402	0.01661	0.05982
Children 1-2 yrs old	0.00931	0.03261	0.12403
Children 3-5 yrs old	0.00688	0.02717	0.10643
Children 6-12 yrs old	0.00328	0.01515	0.06653
Children 13-19 yrs old	0.00137	0.00762	0.03755
Adults 20-49 yrs old	0.00130	0.00714	0.03410
Adults 50+ yrs	0.00178	0.00879	0.03748
Females 13-49 yrs old	0.00139	0.00792	0.03780
SHEDS-Dietary results (150 iterations)			
	95th Pctile	**99th Pctile**	**99.9 Pctile**
Subpopulation	**(mg/kg/day)**	**(mg/kg/day)**	**(mg/kg/day)**
U.S. General	0.0021	0.0108	0.0476
All Infants (< 1 yr)	0.0037	0.0158	0.0556
Children 1-2 yrs old	0.0094	0.0326	0.1228
Children 3-5 yrs old	0.0070	0.0272	0.1041
Children 6-12 yrs old	0.0034	0.0154	0.0697
Children 13-19 yrs old	0.0014	0.0078	0.0361
Adults 20-49 yrs old	0.0013	0.0071	0.0323
Adults 50+ yrs	0.0018	0.0086	0.0365
Females 13-49 yrs old	0.0014	0.0079	0.0358
Ratio (DEEM-FCID/SHEDS)			
	95th Pctile	**99th Pctile**	**99.9 Pctile**
Subpopulation	**(mg/kg/day)**	**(mg/kg/day)**	**(mg/kg/day)**
U.S. General	0.99	1.00	1.02
All Infants (< 1 yr)	1.09	1.05	1.07
Children 1-2 yrs old	0.99	1.00	1.01
Children 3-5 yrs old	0.97	0.99	1.02
Children 6-12 yrs old	0.97	0.98	0.95
Children 13-19 yrs old	0.97	0.97	1.03
Adults 20-49 yrs old	0.99	1.00	1.05
Adults 50+ yrs	1.01	1.02	1.02
Females 13-49 yrs old	0.98	0.99	1.05

In addition to comparing exposures in Table 2-8, we compared SHEDS-Dietary and DEEM results for contribution of exposure from major commodities. Table 2-9 shows that these results are also very similar.

Table 2-9. Contribution to exposure by commodities for 1-2 year-olds.

comcode	Commodities	Percentage DEEM	SHEDS
95003590	Strawberry	34.5	40.3
12002600	Peach	13.0	8.9
95001750	Grape	10.8	13.1
11000070	Apple, fruit with peel	7.6	8.2
95003600	Strawberry, juice	7.2	6.5
12002300	Nectarine	3.7	4.5
11000100	Apple, juice	3.3	2.9
12002850	Plum	2.7	0.8
95001780	Grape, raisin	2.6	2.7
12002880	Plum, prune, juice	2.1	3.0
12002620	Peach juice	1.4	0.0
12000130	Apricot, dried	1.2	1.2
4013550	Spinach	1.1	0.3
95001760	Grape, juice	0.9	1.5
9013990	Watermelon	0.8	1.2
9023560	Squash, summer	0.8	0.1
9021350	Cucumber	0.7	0.0
11002660	Pear	0.6	0.4

Figure 2-11 plots the DEEM-FCID and (cross-sectional) SHEDS-Dietary estimates of exposure at the per capita 99.9th for 17 different drinking water scenarios, for 9 age groups. This plot suggests that these two models produce similar results across many different drinking water scenarios, because the correlation is near 1 (line at near 45 degree angle). For any particular scenario, the infant subpopulation (pink) has the highest exposures (mg ai/kg bw/day) since infants generally have higher drinking water intakes as a percent of their bodyweight (mL/kg bw/day).

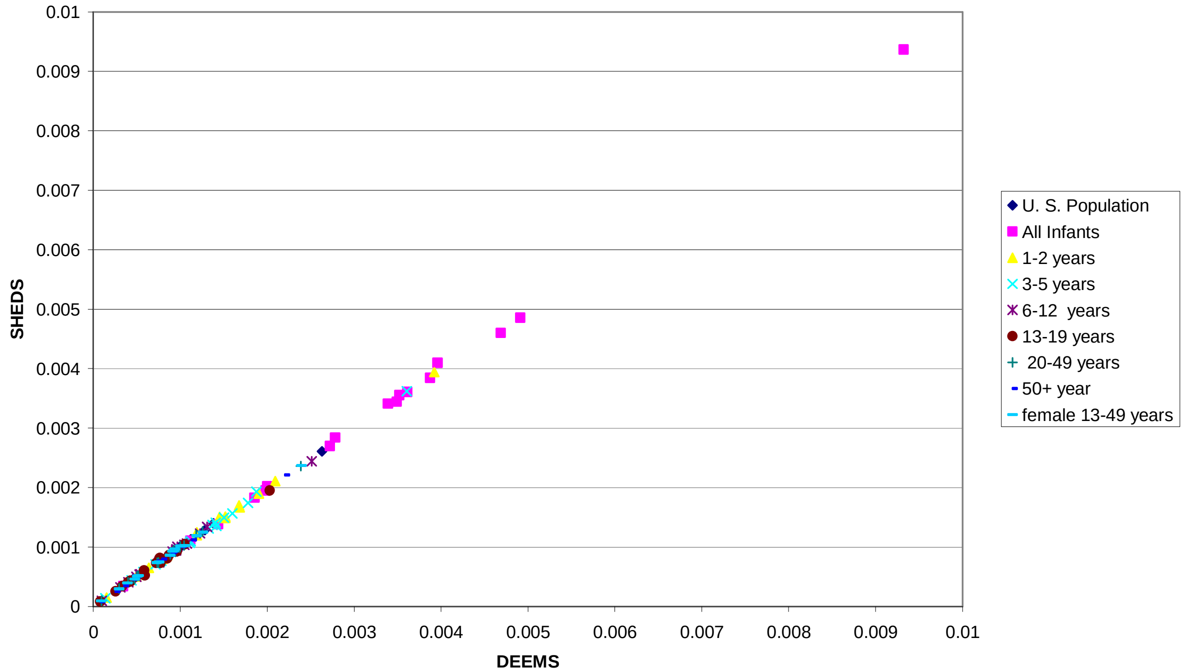


Figure 2-11. Comparison of SHEDS and DEEM on 99.9th percentiles of drinking water. Chemical ABC exposure (mg/kg/day) of 17 different scenarios.

3 Applications/Case Studies to Date

ORD and OPP scientists collaborated to refine, evaluate (compare with DEEM model), and apply the SHEDS dietary module (food and drinking water) for a number of analyses (food and drinking water scenarios, half-life and eating occasion sensitivity analyses, longitudinal simulations with half-life and eating occasion analyses, examining various ways of sampling residues for sensitivity analyses, analyses for contribution by crops and chemicals to identify key risk contributors and help assess risk mitigation scenarios) to refine OPP's risk assessments and inform their risk management decisions for the following:

Aldicarb RED (2006)

- development/testing of eating occasion analyses
- allowed comparison to DEEM-based analyses
- applied Bayer DWCS data (little difference) for direct water intake

Carbaryl (2007)

- explored longitudinal (multi-day) eating occasion analyses (DW-infants, 5+ hrs)

N-Methyl Carbamate CRA (2007)

- supported contention that not significantly overestimating risk by not accounting for recovery (food-only)
- maximum exposure, by eating occasion, provides best case scenario for recovery

Organophosphates CRA (2009-2011)

- updating the 2006 OP Cumulative Risk Assessment
- SHEDS longitudinal eating occasion analysis used to consider persisting effects (carry-over) on AChE inhibition using chemical-specific recovery (half-life) rates
- SHEDS contribution analyses allowed assessing effects of mitigation options on the population 99.9th percentile

EPA/ORD scientists have also applied SHEDS-Dietary to As and MeHg case studies for research purposes, to answer questions about ranges of population exposures, major food contributors, differences in exposures for vulnerable populations, and evaluation of modeled estimates against duplicate food and biomarker data.

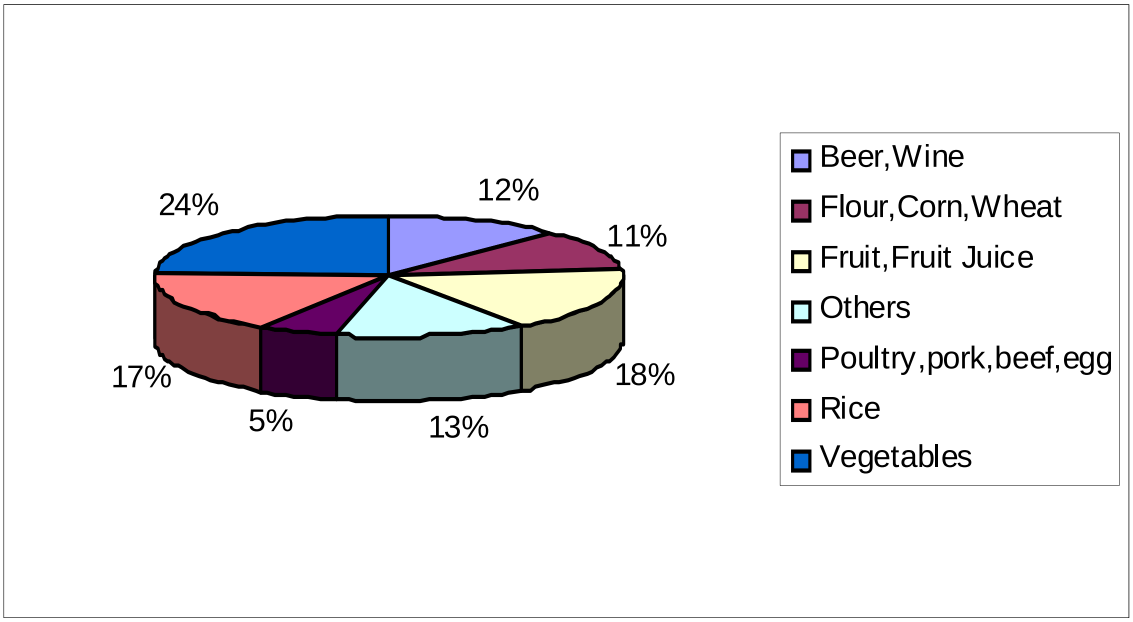
3.1 Arsenic (As)

Dietary exposure from food to toxic inorganic arsenic (iAs) in the general US population has not been well studied. This SHEDS-Dietary research quantifies dietary As exposure, and analyzes the major contributors to total As and iAs. Another objective was to compare model predictions to observed data using both duplicate diet data and (after linkage with a PBPK model) biomarker data.

Probabilistic exposure modeling for dietary As was conducted with the SHEDS-Dietary model, using NHANES/WWEIA consumption data and TDS residue data. The dose modeling was conducted by combining the SHEDS-Dietary model with a physiologically-based pharmacokinetic (PBPK) model in EOHSI's MENTOR-3P system (Xue et al., 2010). Model evaluation was conducted via comparing exposure and dose modeling predictions against NHEXAS duplicate diet data and NHANES biomarker measurements, respectively, for the same individuals.

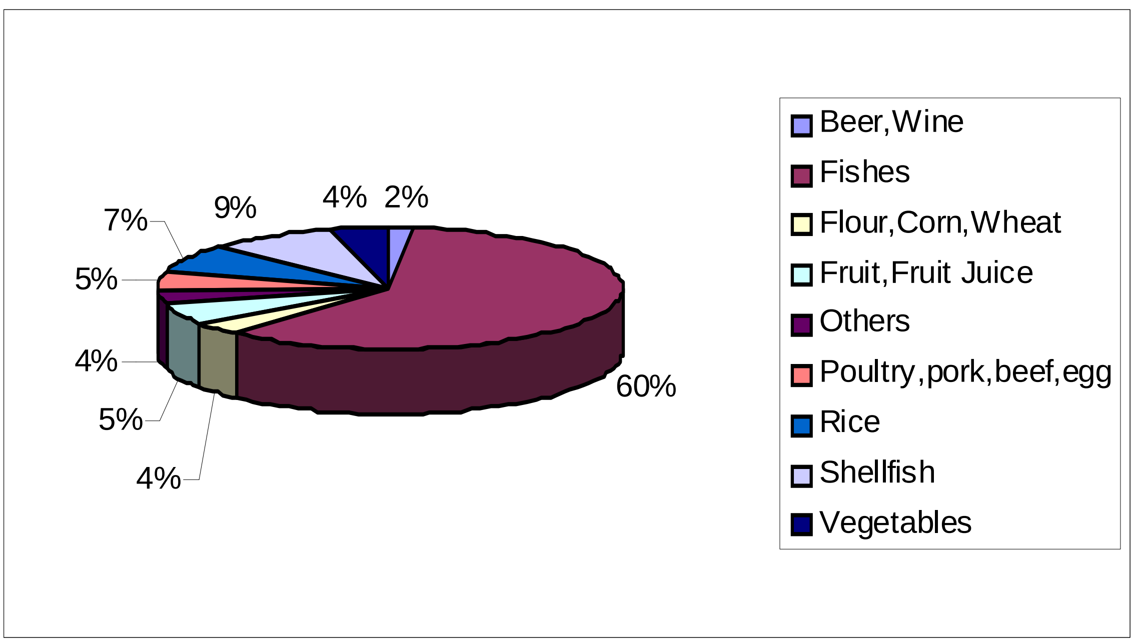
The Xue et al., 2010 SHEDS-Dietary publication revealed that toxic inorganic As (iAs) exposure from food is more important than drinking water for the U.S.. The major food contributors to iAs exposure were vegetables, fruit juices, and fruits; rice; beer and wine; and flour, corn, and wheat (Figure 3-1). The major food contributor for tAS exposure is fish (contributing 60% of exposure; Figure 3-2). The mean modeled tAs exposure from food is 0.38 μg /kg/day, ~14 times higher than the mean As exposures from the drinking water. The mean iAs exposure from food is 0.05 μg /kg/day (1.96 μg /day), ~2 times higher than the mean iAs exposures from the drinking water. Approximately 10% of tAs exposure from foods is the toxic iAs form. SHEDS modeled exposure and dose estimates matched well with the duplicate diet data and measured As biomarkers (Figures 3-3 and 3-4). This model evaluation effort provides more confidence in the exposure assessment tools used, including SHEDS-Dietary.

Some key results are shown in Figures 3-1 to 3-4:



Source: Xue et al., *EHP* 2010

Figure 3-1. Contribution of Inorganic Arsenic Intake by Foods



Source: Xue et al., *EHP* 2010

Figure 3-2. Contribution of Total Arsenic Intake by Foods

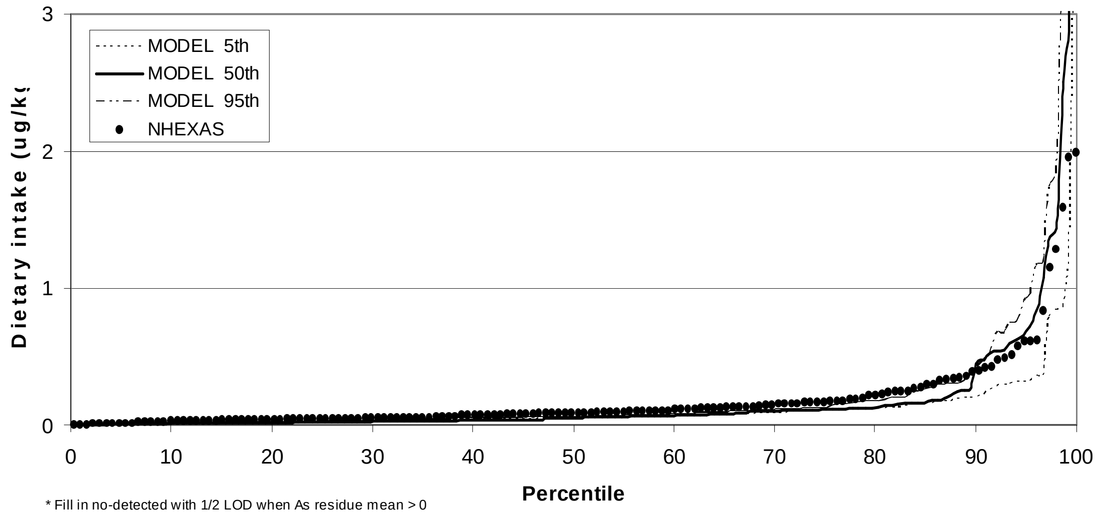
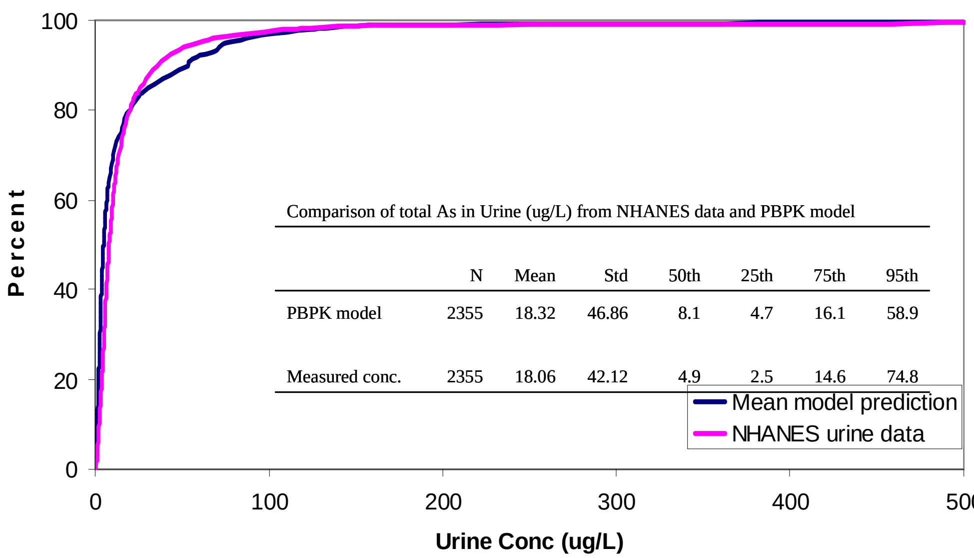


Figure 3-3. SHEDS-Dietary Exposure Model Evaluation for Arsenic Against Duplicate Food Data



Source: Xue et al., *EHP* 2010

Figure 3-4. Total Arsenic Model Evaluation for SHEDS-Dietary linked with MENTOR PBPK Model and Compared Against NHANES Urinary Biomarker Data.

3.1.1 Arsenic Uncertainty Analysis Results

SHEDS-Dietary has a simple bootstrapping method for conducting uncertainty analyses - utilizing only a subset of the consumption and residue data inputs. The SHEDS-Dietary bootstrap procedure applied to Arsenic involved the following steps:

1) Randomly draw certain percentage (1/20 or 5%) of person-day from CSFII data or/and randomly draw certain percentage (1/4 or 25%) of residue data from pollutant residue files by raw commodity and food form,
2) Perform Monte Carlo simulations (e.g., 100 iterations per diary using cross-sectional method)
3) Get population based statistic from each run (e.g., aggregate exposure at per capita 99th percentile)
4) Repeat the steps 1-3 many times, say 200 times
5) Conduct uncertainty analyses from different runs (e.g. will have 200 estimates of the level of aggregate exposure at the per capita 50th, 95th and 99th percentiles, respectively). For each population based statistics (e.g., per capita 99th percentile), the ratio of 95th vs. 5th percentile can be used to evaluate the uncertainty. The bigger the uncertainty ratio, the bigger uncertainty produced by subsets of dietary and residue data.

Figure 3-5 shows the uncertainty for 3 selected percentiles (see Xue et al., 2006 for details on this type of uncertainty analysis), and that 99th percentile has the biggest uncertainty. It presents uncertainty results for daily dietary arsenic exposure, based on bootstrapping 1/30 of CSFII diaries 200 times and 1/8 of the residues. For each percentile, such as 50th, 90th or 95th, there are 200 values, from which the 95th and 5th percentile were acquired and its ratio was calculated. The ratio of the 95th to 5th percentile is 1.19 for 50th percentile; 1.93 and 3.28 for 95th and 99th percentile respectively. We can see that there is relatively little uncertainty regarding the estimate of the 50th percentile as compared to higher percentiles with respect to the amount of residue and consumption data used in the exposure assessment. For the arsenic case study, we performed such bootstrap procedure and calculate 95th/5th ratios for various subsets of consumption and residue data to evaluate the relative contributions to the overall uncertainty.

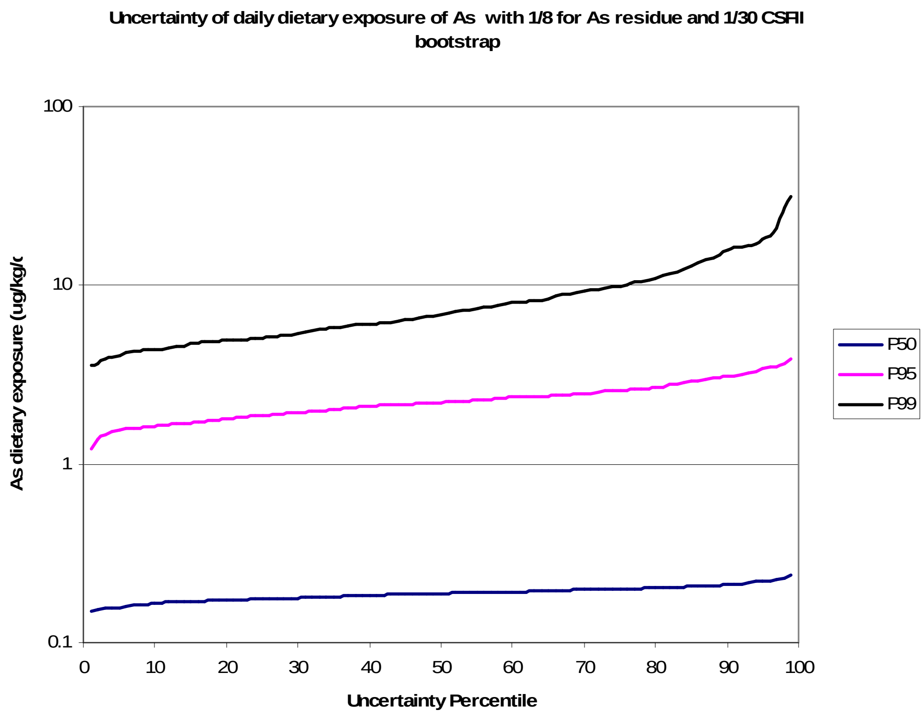


Figure 3-5. Example SHEDS-Dietary Uncertainty Analyses

3.2 Methyl Mercury from Fish Consumption (MeHg)

The MeHg case study examines exposures for vulnerable populations. Asians, Native Americans, and Pacific Islanders (A/N/P) have shown higher levels of MeHg in previous NHANES; reasons have not been well studied. The objectives of this research are to examine dietary exposures to MeHg through fish consumption in different racial/ethnic groups, and extend previous NHANES blood level analyses.

Probabilistic exposure modeling for dietary MeHg was conducted with SHEDS-Dietary, using NHANES/WWEIA fish consumption data and FDA TDS fish residue data. MeHg exposures by race/ethnicity, age group, and food type were analyzed. For Asians, Native Americans, and Pacific Islanders, major contributors for MeHg are tuna, fresh water fish–other, seawater fish–other. Statistical analyses of blood MeHg levels by race/ethnicity from 1999-2006 are being compared against previous published results for 1999-2002 data (6 times larger sample size). Exposure estimates for MeHg in fish can explain the high level of MeHg in blood for populations with higher fish consumption.

Results are shown in Figures 3-6 and 3-7, and Tables 3-1 to 3-2. For all age groups, the A/N/P group has higher mean dietary MeHg exposures than the general population (Figure 3-6 and Table 3-1). 1-2 year-olds and A/N/P have the highest ratio of SHEDS modeled MeHg exposure and NHANES MeHg blood levels. For A/N/P, 5 major contributors for MeHg are tuna, fresh water fish–other, seawater fish–other, salmon, and catfish (Figure 3-7). SHEDS exposure predictions correlate well with NHANES blood biomarker levels in terms of age, gender, and ethnicity. Percentage of MeHg blood levels higher than critical health-based concentrations is higher (up to 8x) for A/N/P compared to other racial/ethnic groups (Table 3-2).

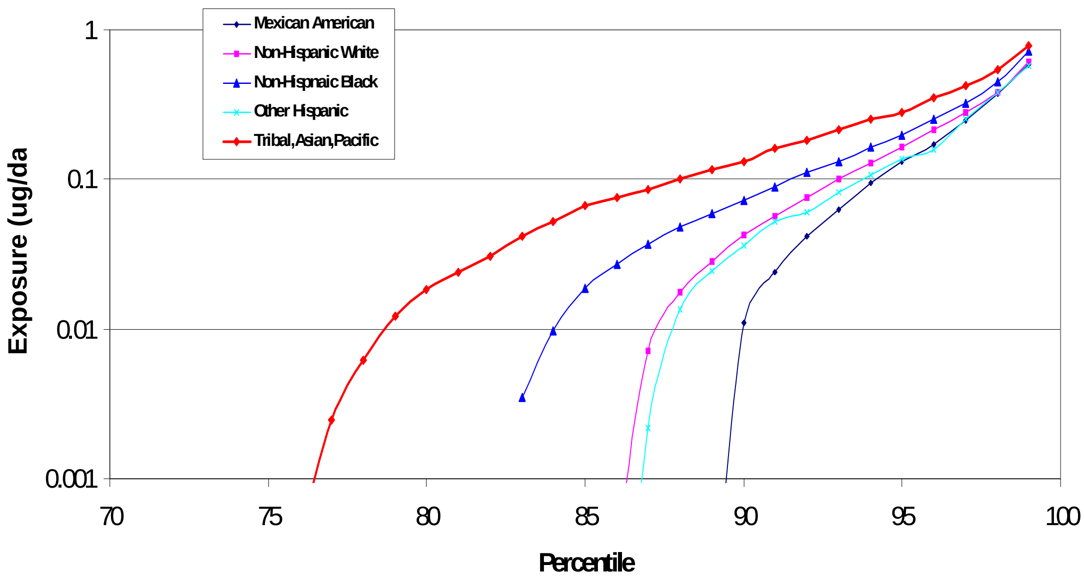


Figure 3-6. SHEDS-Dietary Methyl Mercury Exposure by Ethnicity Using 1999-2006 NHANES Data

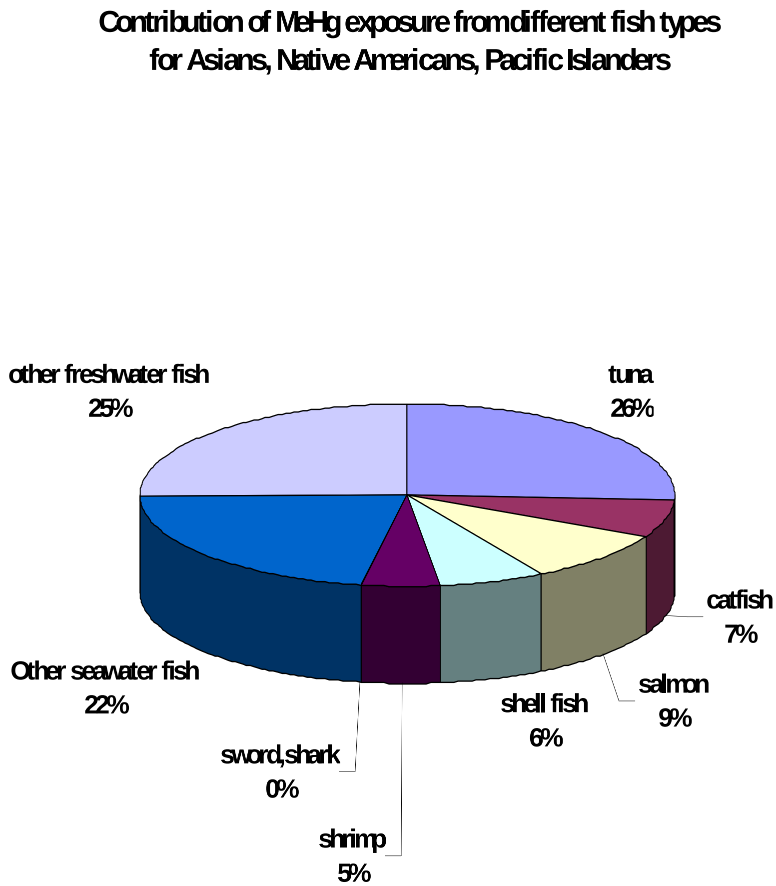


Figure 3-7. Contribution of Methyl Mercury Exposure from Different Fish Types for Asians, Native Americans, and Pacific Islanders Self-Reported in NHANES

Table 3-1. SHEDS-Dietary Methyl Mercury Exposure by Ethnicity and Age from 1999-2006 NHANES Data

			ug/day					ug/kg/day				
Ethnicity	Age	N	Mean	fold	Std	P95	P99	Mean	fold	Std	P95	P99
ANP	0 < 1	170	0.1	1.7	64	0.0	4.9	0.01	1.6	6	0.00	0.53
	1 to <2	89	1.7	5.7	804	7.3	42.0	0.13	4.9	62	0.62	3.09
	2 to <3	96	0.9	1.7	307	8.2	14.9	0.07	1.9	23	0.54	1.13
	3 to <6	200	0.8	1.1	542	3.3	25.8	0.05	1.2	35	0.18	1.61
	6 to <11	285	1.7	1.6	1279	9.6	32.2	0.05	1.5	39	0.20	1.09
	11 to <16	316	0.7	0.7	459	6.5	13.0	0.01	0.8	9	0.11	0.27
	16 to <21	296	2.1	1.8	1565	14.8	34.2	0.03	2.1	25	0.17	0.70
	21 to <50	604	3.8	1.6	2843	20.7	55.3	0.05	1.8	39	0.29	0.78
	50+	366	4.6	1.8	3896	21.9	73.0	0.06	1.8	52	0.30	0.68
REST	0 < 1	2517	0.1		69	0.0	1.3	0.01		8	0.00	0.14
	1 to <2	1704	0.3		228	1.0	8.7	0.03		21	0.10	0.77
	2 to <3	1622	0.5		419	2.1	11.5	0.04		32	0.14	0.77
	3 to <6	3153	0.7		592	3.9	21.3	0.04		31	0.22	1.08
	6 to <11	4815	1.0		856	4.0	28.3	0.03		29	0.13	1.04
	11 to <16	7305	1.0		744	4.6	25.9	0.02		14	0.10	0.49
	16 to <21	6721	1.1		845	5.0	25.3	0.02		11	0.08	0.38
	21 to <50	13211	2.3		2895	12.8	46.7	0.03		37	0.16	0.60
	50+	11530	2.6		2101	15.9	45.9	0.03		29	0.21	0.59

Table 3-2 Summary statistics of organic blood level by age group and ethnicity (µg/liter) from 1999-2006 NHANES data

Ethnicity	Age (yr)	N	Mean	fold	Std	P95	P99
ANP	1 to <2	36	0.76	3.0	133	4.40	4.40
	2 to <3	42	0.59	2.2	102	2.21	4.00
	3 to <6	91	0.57	1.5	182	3.40	6.82
	6 to <11	96	1.01	2.7	277	4.40	6.80
	11 to <16	94	0.69	1.5	152	3.03	4.70
	16 to <21	126	1.24	2.0	244	4.90	6.71
	21 to <50	270	1.69	1.6	421	5.52	6.63
	50+	108	1.70	1.4	374	5.03	5.78
REST	1 to <2	716	0.25		56	0.92	2.46
	2 to <3	726	0.27		57	1.10	2.42
	3 to <6	1570	0.38		99	1.62	3.60
	6 to <11	1336	0.38		93	1.40	3.63
	11 to <16	2089	0.45		91	1.76	4.35
	16 to <21	3117	0.62		116	2.32	5.20
	21 to <50	6339	1.04		281	3.81	6.30
	50+	3510	1.18		253	4.00	6.00

This research extends and is consistent with findings from previous studies focusing on higher blood levels in A/N/P populations, by examining dietary exposures to MeHg from fish consumption. A/N/P populations are exposed to higher levels of MeHg from fish consumption than the general US population and other ethnicity groups. SHEDS-Dietary modeling allows identification of Hg intakes by age, gender, ethnicity, and type of fish. Correlations of modeled dietary exposure predictions with NHANES blood biomarker levels suggest that fish consumption is a key exposure pathway for these populations.

3.3 Permethrin

ORD and OPP scientists have collaborated on application of SHEDS-Dietary to estimate permethrin dietary exposure to support OPP's pyrethroid cumulative risk assessment. The objectives of this SHEDS-Dietary application are to quantify dietary permethrin exposures in the U.S. population, analyze the major contributors, and compare model predictions to observed data using duplicate diet data from the EPA's Children's Total Exposure to Persistent Pollutants study (CTEPP).

CSFII 1994-1996,1998 consumption data and PDP data for residues were used. Model predictions were evaluated against CTEPP duplicate food data for cis- and trans-permethrin (matched SHEDS and CTEPP data by age and gender). A bootstrap approach was applied to assess uncertainty and relative importance of dietary consumption vs. residue data. SHEDS-Dietary was linked to PBPK models and results compared against NHANES biomonitoring data.

Results are as follows and shown in the Tables 3-3 to 3-5 and Figures 3-8 to 3-10 below:

- exposure: 0.44 to 2.2 µg /day; as age increases, exposure increases
- by body weight, young children and 50+yrs. have highest exposure
- 3 most important contributors overall: spinach, lettuce, cabbage
- for 98.5 to 99.5 %ile, lettuce more important
- results similar for cis- and trans-permethrin
- results similar using NHANES vs. CSFII
- SHEDS model results and CTEPP measurement results matched well.

Using the SHEDS-Dietary model, the mean cis-permethrin exposure for the U.S. population from food and drinking water ranged from 0.44 to 2.2 µg /day; 3.4E-05 to 9.9E-5 mg/kg/day. The 95th percentiles ranged from 0.90 to 24.48 µg /day; 8.3E-6 to 6.8E-5 mg/kg/day. As Table 3-3 also shows, as age increases, exposure increases; normalizing by body weight, young children and adults over 50 years have the highest exposures. Results were similar for cis- and trans-permethrin. The three most important contributors overall were spinach (48% cis-), cabbage (28% cis-), and lettuce (10% cis-). For the upper tails of the exposed population (98.5%ile to 99.5 %ile), lettuce was more important (43% cis-; see Figure 3-8).

In comparing with CTEPP measurement results, SHEDS-Dietary exposure estimates (246 paired comparisons) for mean, 95th, and 99th percentiles matched well: the cloud of 100 yellow variability lines from the model contain the observed data in Figure 3-9, and the ratio of modeled to measured data is close to 1 in Table 3-4 for both for cis- and trans- permethrin.

Figure 3-10 and Table 3-5 show the sensitivity of results to which consumption database is used: CSFII or NHANES. Table 3-5 shows that with the NHANES data, lettuce is the most consumed (39.7%) and greatest food contributor to dietary cis-permethrin exposure (47.5% in the % exposure column); using CSFII spinach was the most consumed (37.9% in the % food column) and greatest food contributor to dietary cis-permethrin exposure (46%). The list of key RAC is also different, e.g. apple juice appears in NHANES but not CSFII. Figure 3-10 illustrates the differences in exposure CDFs using the two different consumption databases.

The model evaluation effort with this case study provides more confidence in SHEDS-Dietary. More research is needed with PBPK linkage and model evaluation.

Table 3-3. Cis-permethrin exposure by age groups from SHEDS-Dietary with CSFII Data

		ug/day				mg/kg/day			
age group	n	mean	std	p95	p99	mean	std	p95	p99
0 < 1 years	297200	6.7E-01	4.7E+02	7.7E-02	1.1E+01	7.9E-05	5.6E-02	8.3E-06	1.3E-03
1-2 years	419200	4.4E-01	3.8E+02	5.1E-01	6.0E+00	3.9E-05	3.7E-02	4.0E-05	4.7E-04
3-5 years	878200	5.2E-01	4.2E+02	7.8E-01	8.0E+00	3.0E-05	2.4E-02	4.4E-05	4.4E-04
6-12 years	417800	7.0E-01	8.9E+02	1.3E+00	1.3E+01	2.1E-05	2.7E-02	4.1E-05	3.9E-04
13-19 years	244400	1.1E+00	1.6E+03	2.4E+00	1.9E+01	1.6E-05	2.2E-02	3.8E-05	3.0E-04
20-49 years	935400	1.8E+00	2.7E+03	4.2E+00	3.8E+01	2.6E-05	4.1E-02	5.8E-05	5.3E-04
50+ years	929200	2.2E+00	2.3E+03	5.0E+00	4.7E+01	3.2E-05	3.4E-02	6.8E-05	6.6E-04

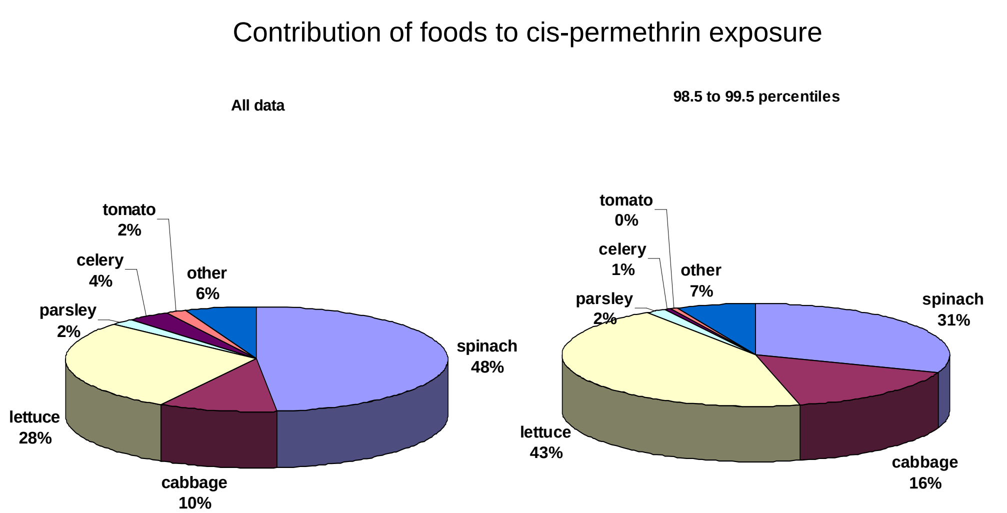


Figure 3-8. Contribution of Foods to Cis-Permethrin Exposure Using SHEDS-Dietary

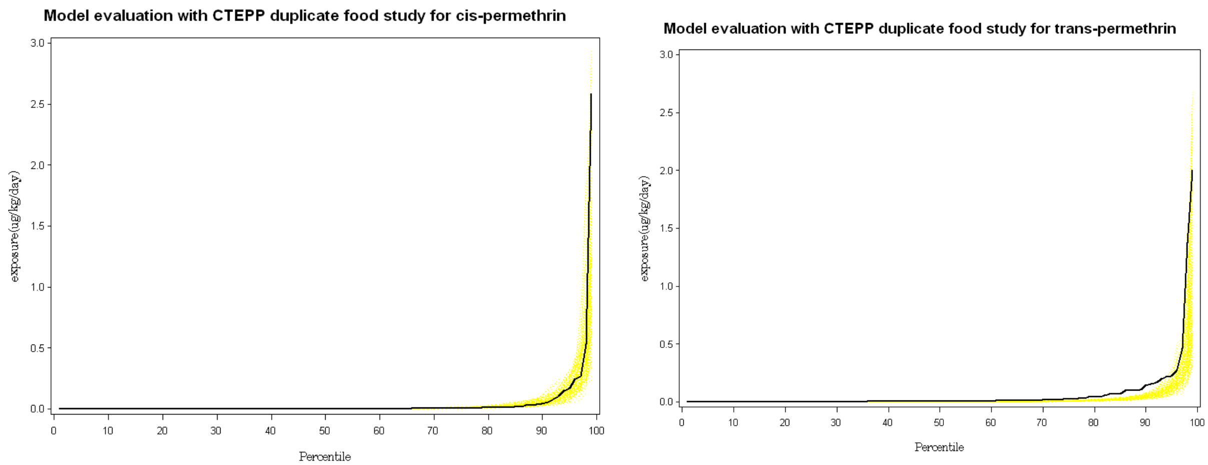


Figure 3-9. Comparison of SHEDS-Dietary Estimates Against CTEPP Duplicate Diet Exposure Data for Cis- and Trans- Permethrin. (Note: The cloud of yellow lines illustrating 100 modeled variability runs contains the observed data.)

Table 3-4. SHEDS-Dietary Evaluation against CTEPP Duplicate Diet Data for Cis- and Trans- Permethrin with CSFII Data

perm	mean	std	p5	p25	p50	p75	p95	p99
SHEDS cis-permethrin	6.9E-02	6.6E-01	4.9E-07	2.6E-05	2.5E-04	9.7E-03	1.7E-01	1.3E+00
CTEPP cis-permethrin	6.5E-02	3.8E-01	4.2E-04	6.8E-04	1.3E-03	5.8E-03	1.7E-01	2.6E+00
SHEDS trans-permethrin	6.8E-02	7.2E-01	0.0E+00	1.8E-05	1.8E-04	8.0E-03	1.5E-01	1.2E+00
CTEPP trans-permethrin	8.9E-02	3.8E-01	1.0E-03	2.2E-03	4.8E-03	2.3E-02	2.2E-01	2.0E+00

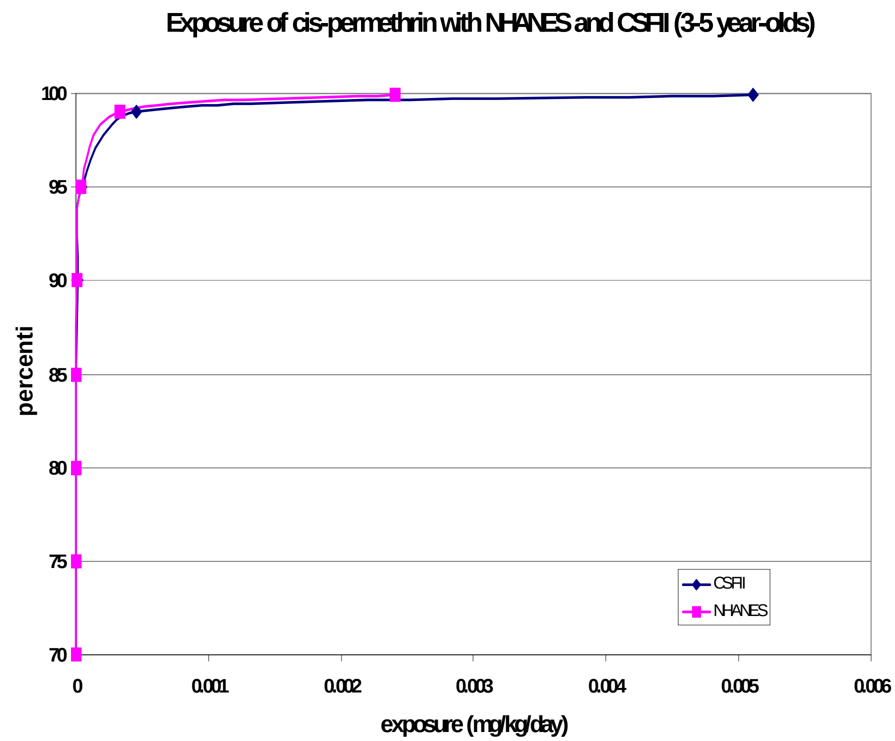


Figure 3-10. SHEDS-Dietary Modeled Exposure of Cis-Permethrin with NHANES and CSFII for 3-5 year-olds

Table 3-5. SHEDS-Dietary Modeled Contribution of RAC to Total Food Consumption for Cis-Permethrin and 3-5 year-olds

Contribution of RAC to total food consumption and cis-permethrin exposure
(3-5 year-olds)

	CSFII			NHANES	
RAC	% food	% exposure	RAC	% food	% exposure
Spinach	37.9	46.0	Lettuce, head	39.7	47.5
Lettuce, head	29.0	34.5	Spinach	12.9	24.0
Cabbage	14.6	11.1	Cabbage	14.0	11.2
Endive	0.7	2.7	Endive	1.7	6.8
Lettuce, leaf	1.7	1.7	Parsley, leaves	0.3	2.7
Parsley, leaves	0.1	0.8	Lettuce, leaf	2.7	2.6
Spinach-babyfood	0.3	0.7	Pear	2.8	0.9
Brussels sprouts	0.8	0.6	Cantaloupe	4.1	0.7
Cantaloupe	3.2	0.4	Tomato	4.4	0.7
Celery	2.2	0.3	Peach	1.7	0.5
Pear	0.8	0.2	Broccoli	2.2	0.5
Peach	0.5	0.2	Watermelon	5.0	0.4
Tomato	1.5	0.2	Pepper, bell	0.7	0.3
Watermelon	2.2	0.1	Brussels sprouts	0.2	0.3
Broccoli	0.8	0.1	Celery	1.5	0.3
Pepper, bell	0.3	0.1	Apple, juice	4.2	0.3

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